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59821

From: Hunt, Jennifer
Sent: Wednesday, February 06, 2002 7:28 PM
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Subject: Seq Search for 09/480,977

Please search and interference search SEQ ID NO:4 of 09/480,977.

Thanks.

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Patent Examiner, Art Unit 1642
CM1-8D06 (mailbox 8E12)
(703)308-7548

Edward Hart
Technical Info Specialist
STIC/Biotech
CM1 12014 Tel: 505-9203

Searcher: _____
Phone: _____
Location: _____
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Searcher Prep/Review: _____
Clerical: _____
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TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST(where applic.)
STN: _____
DIALOG: _____
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DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: 02
WWW/Internet: _____
Other (specify): _____

Thu Feb 7 13:45:28 2002 09/18/01 09/18/01 10/13/01 10/13/01

us-09-480-977-4.ra1

GenCore version 4.5
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OM protein - protein search, using sw model

Run on: February 7, 2002, 12:56:46 ; Search time 12.54 Seconds
(Without alignments)
84.342 Million cell updates/sec

Title: US-09-480-977-4
Perfect score: 277
Sequence: 1 HFKRCRDLAYCLNDEGCF.....SHKHCKEYGVGRCDPFL 47

Scoring table: BIOSUM62
Gapop 10.0, Gapext 0.5

Searched: 212252 seqs, 22503292 residues

Total number of hits satisfying chosen parameters: 212252

Minimum DB seq length: 0
Maximum DB seq length: 200000000

Post-processing: Minimum Match 08
Maximum Match 1008
Listing first 45 summaries

Database : Issued Patents AA:*
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6: /cgn2_6/ptodata/2/1aa/backfilest1.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	277	100.0	47	US-08-899-437-4	Sequence 4, Appl 1
2	277	100.0	47	US-08-899-437-8	Sequence 8, Appl 1
3	277	100.0	47	US-09-126-121-4	Sequence 4, Appl 1
4	277	100.0	47	US-09-126-121-8	Sequence 8, Appl 1
5	277	100.0	47	US-08-899-437-7	Sequence 7, Appl 1
6	277	100.0	47	US-09-126-121-7	Sequence 7, Appl 1
7	277	100.0	47	US-08-899-437-3	Sequence 3, Appl 1
8	277	100.0	47	US-09-126-121-3	Sequence 3, Appl 1
9	277	100.0	47	US-08-899-437-23	Sequence 23, Appl 1
10	277	100.0	47	US-09-126-121-23	Sequence 23, Appl 1
11	277	100.0	47	US-08-899-437-2	Sequence 2, Appl 1
12	277	100.0	47	US-09-126-121-2	Sequence 2, Appl 1
13	277	100.0	47	US-08-899-437-6	Sequence 6, Appl 1
14	277	100.0	47	US-09-126-121-6	Sequence 6, Appl 1
15	277	100.0	47	US-08-417-640A-1	Sequence 1, Appl 1
16	277	100.0	47	US-08-760-815-1	Sequence 1, Appl 1
17	277	100.0	47	US-08-761-038-1	Sequence 1, Appl 1
18	277	100.0	47	US-09-238-182-1	Sequence 1, Appl 1
19	277	100.0	47	US-08-899-437-14	Sequence 14, Appl 1
20	277	100.0	47	US-09-126-121-14	Sequence 14, Appl 1
21	277	100.0	47	US-08-753-007A-12	Sequence 12, Appl 1
22	277	100.0	47	US-09-398-496-12	Sequence 12, Appl 1
23	277	100.0	47	US-08-417-640A-3	Sequence 3, Appl 1
24	277	100.0	47	US-08-760-815-3	Sequence 3, Appl 1
25	277	100.0	47	US-08-761-038-3	Sequence 3, Appl 1
26	277	100.0	47	US-08-179-481-111	Sequence 11, Appl 1
27	277	100.0	47	US-08-341-018-62	Sequence 62, Appl 1

28	113.5	41.0	63	4	US-08-470-335-221	Sequence 221, App
29	113.5	41.0	63	4	US-08-470-339-221	Sequence 221, App
30	113.5	41.0	66	1	US-07-847-743B-10	Sequence 10, Appl
31	113.5	41.0	66	1	US-08-456-201-10	Sequence 10, Appl
32	113.5	41.0	66	2	US-08-456-241-10	Sequence 10, Appl
33	113.5	41.0	66	4	US-09-020-880-2	Sequence 2, Appl 1
34	113.5	41.0	66	5	PCT-US92-04295A-10	Sequence 10, Appl
35	113.5	41.0	83	3	US-08-341-018-70	Sequence 70, Appl
36	113.5	41.0	83	4	US-08-470-335-225	Sequence 225, App
37	113.5	41.0	83	4	US-08-470-339-225	Sequence 225, App
38	113.5	41.0	88	3	US-08-341-018-68	Sequence 68, Appl
39	113.5	41.0	88	4	US-08-470-335-224	Sequence 224, App
40	113.5	41.0	88	4	US-08-470-339-224	Sequence 224, App
41	113.5	41.0	95	1	US-07-847-743B-14	Sequence 14, Appl
42	113.5	41.0	95	1	US-08-456-201-14	Sequence 14, Appl
43	113.5	41.0	95	2	US-08-330-161-12	Sequence 12, Appl
44	113.5	41.0	95	2	US-08-456-241-14	Sequence 14, Appl
45	113.5	41.0	95	2	US-08-440-401-12	Sequence 12, Appl

ALIGNMENTS

RESULT 1
US-08-899-437-4
Sequence 4, Application US/08899437
Patent No. 6121415
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
TITLE OF INVENTION: Ligands and Uses Therefor
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 Inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Winpatin (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/899,437
FILING DATE: 24-Jul-1997
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delaire L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881
INFORMATION FOR SEQ ID NO: 4:
SEQUENCE CHARACTERISTICS:
LENGTH: 47 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: NR3 EGF-like domain/amino acid seq.
LOCATION: 1-47
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-08-899-437-4
Query Match 100.0%; Score 277; DB 3; Length 47;
Best Local Similarity 100.0%; Pred. No. 1.2e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
CY 1 HFKRCRDLAYCLNDEGCFVETLTGSHKHCKEYGVGRCDPFL 47

Db 1 HFKPCRDKLAYCLNDGECFVETLTGSHKRCRCKEGYGVACDQFL 47

RESULT 2
US-08-899-437-8

; Sequence 8, Application US/08899437
; Patent No. 6121415
; GENERAL INFORMATION:
; APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
; TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
; TITLE OF INVENTION: Ligands and Uses Therefor
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Genentech, Inc.
; STREET: 1 DNA Way
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA
; ZIP: 94080
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 3.5 inch, 1.44 MB floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: Winpatin (Genentech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/899,437
; FILING DATE: 24-Jul-1997
; CLASSIFICATION: 435
; ATTORNEY/AGENT INFORMATION:
; NAME: Conley, Delidre L.
; REGISTRATION NUMBER: 36,487
; REFERENCE/DOCKET NUMBER: P1084R1
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 650/225-2066
; TELEFAX: 650/952-9881
; INFORMATION FOR SEQ ID NO: 8:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 47 amino acids
; TYPE: Amino Acid
; TOPOLOGY: Linear
; FEATURE:
; NAME/KEY: NRG3 EGF-like domain/amino acid seq.
; LOCATION: 1-47
; IDENTIFICATION METHOD:
; OTHER INFORMATION:
US-08-899-437-8

Query Match 100.0%; Score 277; DB 3; Length 47;
Best Local Similarity 100.0%; Pred. No. 1.2e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Oy 1 HFKPCRDKLAYCLNDGECFVETLTGSHKRCRCKEGYGVACDQFL 47
Db 1 HFKPCRDKLAYCLNDGECFVETLTGSHKRCRCKEGYGVACDQFL 47

RESULT 3
US-09-126-121-4

; Sequence 4, Application US/09126121
; Patent No. 6252051
; GENERAL INFORMATION:
; APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
; TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
; TITLE OF INVENTION: Ligands and Uses Therefor
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Genentech, Inc.
; STREET: 1 DNA Way
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA

ZIP: 94080

; COMPUTER READABLE FORM:
; MEDIUM TYPE: 3.5 inch, 1.44 MB floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: Winpatin (Genentech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/09/126,121
; FILING DATE: 30-Jul-1998
; CLASSIFICATION:
; ATTORNEY/AGENT INFORMATION:
; NAME: Conley, Delidre L.
; REGISTRATION NUMBER: 36,487
; REFERENCE/DOCKET NUMBER: P1084R1D1
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 650/225-2066
; TELEFAX: 650/952-9881
; INFORMATION FOR SEQ ID NO: 4:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 47 amino acids
; TYPE: Amino Acid
; TOPOLOGY: Linear
; FEATURE:
; NAME/KEY: NRG3 EGF-like domain/amino acid seq.
; LOCATION: 1-47
; IDENTIFICATION METHOD:
; OTHER INFORMATION:
US-09-126-121-4

Query Match 100.0%; Score 277; DB 4; Length 47;
Best Local Similarity 100.0%; Pred. No. 1.2e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Oy 1 HFKPCRDKLAYCLNDGECFVETLTGSHKRCRCKEGYGVACDQFL 47
Db 1 HFKPCRDKLAYCLNDGECFVETLTGSHKRCRCKEGYGVACDQFL 47

RESULT 4
US-09-126-121-8

; Sequence 8, Application US/09126121
; Patent No. 6252051
; GENERAL INFORMATION:
; APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
; TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
; TITLE OF INVENTION: Ligands and Uses Therefor
; NUMBER OF SEQUENCES: 23
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Genentech, Inc.
; STREET: 1 DNA Way
; CITY: South San Francisco
; STATE: California
; COUNTRY: USA
; ZIP: 94080
; COMPUTER READABLE FORM:
; MEDIUM TYPE: 3.5 inch, 1.44 MB floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: Winpatin (Genentech)
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/09/126,121
; FILING DATE: 30-Jul-1998
; CLASSIFICATION:
; ATTORNEY/AGENT INFORMATION:
; NAME: Conley, Delidre L.
; REGISTRATION NUMBER: 36,487
; REFERENCE/DOCKET NUMBER: P1084R1D1
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 650/225-2066
; TELEFAX: 650/952-9881
; INFORMATION FOR SEQ ID NO: 8:
; SEQUENCE CHARACTERISTICS:

LENGTH: 47 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: NRG3 EGF-like domain/amino acid seq.
LOCATION: 1-47
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-09-126-121-8

Query Match 100.0%; Score 277; DB 4; Length 47;
Best Local Similarity 100.0%; Pred. No. 1.2e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAVCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 47
Db 1 HFKPCRDKLAVCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 47

RESULT 5
US-08-899-437-7
Sequence 7, Application US/08899437
Patent No. 6121415
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
TITLE OF INVENTION: Ligands and Uses Therefor
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Winpatin (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/899,437
FILING DATE: 24-Jul-1997
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881
INFORMATION FOR SEQ ID NO: 7:
SEQUENCE CHARACTERISTICS:
LENGTH: 360 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: hNRG3 extracellular domain/Amino AcidSeq
LOCATION: 1-360
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-08-899-437-7

Query Match 100.0%; Score 277; DB 3; Length 360;
Best Local Similarity 100.0%; Pred. No. 9.6e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAVCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 47
Db 286 HFKPCRDKLAVCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 332

RESULT 6
US-09-126-121-7
Sequence 7, Application US/09126121
Patent No. 6252051
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
TITLE OF INVENTION: Ligands and Uses Therefor
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Winpatin (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/126,121
FILING DATE: 30-Jul-1998
CLASSIFICATION:
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1D1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881
INFORMATION FOR SEQ ID NO: 7:
SEQUENCE CHARACTERISTICS:
LENGTH: 360 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: hNRG3 extracellular domain/Amino AcidSeq
LOCATION: 1-360
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-09-126-121-7

Query Match 100.0%; Score 277; DB 4; Length 360;
Best Local Similarity 100.0%; Pred. No. 9.6e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAVCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 47
Db 286 HFKPCRDKLAVCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 332

RESULT 7
US-08-899-437-3
Sequence 3, Application US/08899437
Patent No. 6121415
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
TITLE OF INVENTION: Ligands and Uses Therefor
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk

COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: WinPatIn (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/899,437
FILING DATE: 24-Jul-1997
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/953-9881
INFORMATION FOR SEQ ID NO: 3:
SEQUENCE CHARACTERISTICS:
LENGTH: 362 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: mNRG3 extracellular domain amino acid seq
LOCATION: 1-362
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-08-899-437-3

Query Match 100.0%; Score 277; DB 3; Length 362;
Best Local Similarity 100.0%; Pred. No. 9,6e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAYCLNDGCFYIEITLGSKHCRCKEGYGVRCDFL 47
DB 288 HFKPCRDKLAYCLNDGCFYIEITLGSKHCRCKEGYGVRCDFL 334

RESULT 8
US-09-126-121-3
Sequence 3, Application US/09126121
Patent No. 6252051
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
TITLE OF INVENTION: Ligands and Uses Therefor
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: WinPatIn (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/126,121
FILING DATE: 30-Jul-1998
CLASSIFICATION:
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/953-9881
INFORMATION FOR SEQ ID NO: 3:
SEQUENCE CHARACTERISTICS:
LENGTH: 362 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear

FEATURE:
NAME/KEY: mNRG3 extracellular domain amino acid seq
LOCATION: 1-362
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-09-126-121-3

Query Match 100.0%; Score 277; DB 4; Length 362;
Best Local Similarity 100.0%; Pred. No. 9,6e-26;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAYCLNDGCFYIEITLGSKHCRCKEGYGVRCDFL 47
DB 288 HFKPCRDKLAYCLNDGCFYIEITLGSKHCRCKEGYGVRCDFL 334

RESULT 9
US-08-899-437-23
Sequence 23, Application US/08899437
Patent No. 6121415
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
TITLE OF INVENTION: Ligands and Uses Therefor
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: WinPatIn (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/899,437
FILING DATE: 24-Jul-1997
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881
INFORMATION FOR SEQ ID NO: 23:
SEQUENCE CHARACTERISTICS:
LENGTH: 696 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: Human NRG3B2
LOCATION: 1-696
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-08-899-437-23

Query Match 100.0%; Score 277; DB 3; Length 696;
Best Local Similarity 100.0%; Pred. No. 1,9e-25;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAYCLNDGCFYIEITLGSKHCRCKEGYGVRCDFL 47
DB 286 HFKPCRDKLAYCLNDGCFYIEITLGSKHCRCKEGYGVRCDFL 332

RESULT 10
US-09-126-121-23

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Sequence 23, Application US/09126121
Patent No. 6252051
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSER: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: WinPatIn (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/126,121
FILING DATE: 30-Jul-1998
CLASSIFICATION:
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1D1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/952-9881
TELEFAX: 650/225-2066
INFORMATION FOR SEQ ID NO: 23:
SEQUENCE CHARACTERISTICS:
LENGTH: 696 amino acids
TYPE: Amino acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: Human NRG3B2
LOCATION: 1-696
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-09-126-121-23

Query Match 100.0%; Score 277; DB 4; Length 696;
Best Local Similarity 100.0%; Pred. No. 1.9e-25;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPRKDLAYCLNDGCFYETLTGSHKRCRCKEGYGVRCDFL 47
DB 286 HFKPRKDLAYCLNDGCFYETLTGSHKRCRCKEGYGVRCDFL 332

RESULT 11
US-08-899-437-2
Sequence 2, Application US/08899437
Patent No. 6121415
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSER: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: WinPatIn (Genentech)
```

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CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/899,437
FILING DATE: 24-Jul-1997
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881
INFORMATION FOR SEQ ID NO: 2:
SEQUENCE CHARACTERISTICS:
LENGTH: 713 amino acids
TYPE: Amino acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: Mouse NRG3 (mNRG3)/amino acid seq.
LOCATION: 1-713
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-08-899-437-2

Query Match 100.0%; Score 277; DB 3; Length 713;
Best Local Similarity 100.0%; Pred. No. 1.9e-25;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPRKDLAYCLNDGCFYETLTGSHKRCRCKEGYGVRCDFL 47
DB 288 HFKPRKDLAYCLNDGCFYETLTGSHKRCRCKEGYGVRCDFL 334

RESULT 12
US-09-126-121-2
Sequence 2, Application US/09126121
Patent No. 6252051
GENERAL INFORMATION:
APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSER: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080
COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: WinPatIn (Genentech)
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/126,121
FILING DATE: 30-Jul-1998
CLASSIFICATION:
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1D1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/952-9881
TELEFAX: 650/225-2066
INFORMATION FOR SEQ ID NO: 2:
SEQUENCE CHARACTERISTICS:
LENGTH: 713 amino acids
TYPE: Amino acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: Mouse NRG3 (mNRG3)/amino acid seq.
LOCATION: 1-713
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IDENTIFICATION METHOD:
OTHER INFORMATION:

Query Match 100.0%; Score 277; DB 4; Length 713;
Best Local Similarity 100.0%; Pred. No. 1.9e-25;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 HFKPCRDKLAVCLNDGECFVETLTGSHKRCCKEGYGVRCDFL 47
DB 288 HFKPCRDKLAVCLNDGECFVETLTGSHKRCCKEGYGVRCDFL 334

RESULT 13

US-08-899-437-6
Sequence 6, Application US/08899437 —
Patent No. 6121415

GENERAL INFORMATION:

APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080

COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Winpatin (Genentech)

CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/899,437
FILING DATE: 24-Jul-1997
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881

INFORMATION FOR SEQ ID NO: 6:
SEQUENCE CHARACTERISTICS:
LENGTH: 720 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: hNRG3B1 amino acid sequence
LOCATION: 1-720
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-08-899-437-6

Query Match 100.0%; Score 277; DB 3; Length 720;
Best Local Similarity 100.0%; Pred. No. 1.9e-25;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 HFKPCRDKLAVCLNDGECFVETLTGSHKRCCKEGYGVRCDFL 47
DB 286 HFKPCRDKLAVCLNDGECFVETLTGSHKRCCKEGYGVRCDFL 332

RESULT 14
US-09-126-121-6
Sequence 6, Application US/09126121
Patent No. 6252051
GENERAL INFORMATION:

APPLICANT: Godowski, Paul J., Mark, Melanie Rose, Zhang, Dong Xiao
TITLE OF INVENTION: ErbB Receptor-Specific Neuregulin Related
NUMBER OF SEQUENCES: 23
CORRESPONDENCE ADDRESS:
ADDRESSEE: Genentech, Inc.
STREET: 1 DNA Way
CITY: South San Francisco
STATE: California
COUNTRY: USA
ZIP: 94080

COMPUTER READABLE FORM:
MEDIUM TYPE: 3.5 inch, 1.44 Mb floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Winpatin (Genentech)

CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/09/126,121
FILING DATE: 30-Jul-1998
CLASSIFICATION:
ATTORNEY/AGENT INFORMATION:
NAME: Conley, Delidre L.
REGISTRATION NUMBER: 36,487
REFERENCE/DOCKET NUMBER: P1084R1D1
TELECOMMUNICATION INFORMATION:
TELEPHONE: 650/225-2066
TELEFAX: 650/952-9881

INFORMATION FOR SEQ ID NO: 6:
SEQUENCE CHARACTERISTICS:
LENGTH: 720 amino acids
TYPE: Amino Acid
TOPOLOGY: Linear
FEATURE:
NAME/KEY: hNRG3B1 amino acid sequence
LOCATION: 1-720
IDENTIFICATION METHOD:
OTHER INFORMATION:
US-09-126-121-6

Query Match 100.0%; Score 277; DB 4; Length 720;
Best Local Similarity 100.0%; Pred. No. 1.9e-25;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 HFKPCRDKLAVCLNDGECFVETLTGSHKRCCKEGYGVRCDFL 47
DB 286 HFKPCRDKLAVCLNDGECFVETLTGSHKRCCKEGYGVRCDFL 332

RESULT 15
US-08-417-640A-1
Sequence 1, Application US/08417640A
Patent No. 5670342
GENERAL INFORMATION:
APPLICANT: Carnahan, Josette F.
APPLICANT: Hara, Shintichi
APPLICANT: Lu, Hsiang S.
APPLICANT: Mayer, John P.
APPLICANT: Yoshinaga, Steven K.
TITLE OF INVENTION: NDF Peptides
NUMBER OF SEQUENCES: 6
CORRESPONDENCE ADDRESS:
ADDRESSEE: Amgen Inc.
STREET: 1840 Dehavenland Drive
CITY: Thousand Oaks
STATE: California
COUNTRY: USA
ZIP: 91320

COMPUTER READABLE FORM:
MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: PatentIn Release #1.0, Version #1.25

GenCore version 4.5
Copyright (c) 1993 - 2000 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: February 7, 2002, 12:54:46 ; Search time 23.88 Seconds
(without alignments)
145.789 Million cell updates/sec

Title: US-09-480-977-4

Sequence: 1 HKPRDMDLAVCLNDGEF.....SHKHCRKRGYGVRCDFL 47

Scoring table:

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Gapop 10.0 , Gapext 0.5

Searched:

522463 seqs, 74073290 residues

Total number of hits satisfying chosen parameters: 522463

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing:

Minimum Match 08
Maximum Match 1008
Listing first 45 summaries

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- 2: /SIDSR/gcgdata/geneseq/AA1981.DAT:*
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- 21: /SIDSR/gcgdata/geneseq/AA2000.DAT:*
- 22: /SIDSR/gcgdata/geneseq/AA2001.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	277	100.0	47	AAW97622	Human neuroguilin r
2	277	100.0	157	AAW05451	Human hereguilin-11
3	277	100.0	360	AAW97621	Human neuroguilin r
4	277	100.0	362	AAW97620	Mouse neuroguilin r
5	277	100.0	696	AAW97619	Human neuroguilin r
6	277	100.0	713	AAW97617	Mouse neuroguilin r
7	277	100.0	720	AAW05452	Human hereguilin-11
8	277	100.0	720	AAW97618	Human neuroguilin r
9	116.5	42.1	52	AAW05182	Human NDF EGF-like
10	116.5	42.1	52	AAW12602	Human NDF EGF-like
11	116.5	42.1	21	AAW69983	NDF/heregulin prot

12	113.5	41.0	52	17	AAW05184	Neu differentiatio
13	113.5	41.0	63	15	AAW46918	EGF12. AAR46918
14	113.5	41.0	63	15	AAW55659	EGF12. AAR55659
15	113.5	41.0	63	16	AAW67250	Human epidermal 11
16	113.5	41.0	63	17	AAW09363	EGF12. Not specif
17	113.5	41.0	63	17	AAW96076	Epidermal growth f
18	113.5	41.0	63	17	AAW87461	Epidermal growth f
19	113.5	41.0	66	21	AAW36702	EGF-like domain of
20	113.5	41.0	83	15	AAW46922	EGF16. AAR46922
21	113.5	41.0	83	15	AAW55663	EGF16. AAR55663
22	113.5	41.0	83	16	AAW67254	EGF16. AAR67254
23	113.5	41.0	83	17	AAW09367	Human epidermal 11
24	113.5	41.0	83	17	AAW96080	EGF16. Not specif
25	113.5	41.0	83	17	AAW87465	Epidermal growth f
26	113.5	41.0	88	15	AAW46921	EGF15. AAR46921
27	113.5	41.0	88	15	AAW55662	EGF15. AAR55662
28	113.5	41.0	88	16	AAW67253	Human epidermal 11
29	113.5	41.0	88	17	AAW09366	EGF15. Not specif
30	113.5	41.0	88	17	AAW96079	Epidermal growth f
31	113.5	41.0	88	17	AAW87464	Epidermal growth f
32	113.5	41.0	125	16	AAW68564	Human NDF-alpha3 c
33	113.5	41.0	263	13	AAW28537	GGF2BPP2. CDS prote
34	113.5	41.0	263	13	AAW46896	GGF2BPP2. Bos tau
35	113.5	41.0	263	15	AAW55689	GGF2BPP2. Bos tau
36	113.5	41.0	263	16	AAW67217	Putative bovine gl
37	113.5	41.0	263	17	AAW09360	Bovine neuroguilin
38	113.5	41.0	280	15	AAW46915	GGF2BPP2. Bos tau
39	113.5	41.0	280	15	AAW55656	GGF2BPP2. Bos tau
40	113.5	41.0	280	16	AAW67244	Bovine glial cell
41	113.5	41.0	280	17	AAW09369	Human neuroguilin G
42	113.5	41.0	280	17	AAW98762	Glial growth facto
43	113.5	41.0	280	17	AAW87455	Bp2 glial growth
44	113.5	41.0	280	20	AAW26577	Amino acid sequenc
45	113.5	41.0	375	18	AAW06683	Hereguilin-alpha fu

ALIGNMENTS

RESULT 1	AAW97622	standard; protein; 47 AA.
ID	AAW97622;	
AC	AAW97622;	
DT	10-MAY-1999	(first entry)
XX		
DE	Human neuroguilin related ligand NR3 EGF-like domain.	
XX		
KW	Neuroguilin related ligand; NR3; hNR3B1; human; ErbB4 receptor;	
KW	signal transduction; nervous system disorder; neurodegeneration;	
KW	neuropathy; therapy; diagnosis; epidermal growth factor; EGF;	
KW	Immunoadhesion.	
XX		
OS	Homo sapiens.	
XX		
PN	W09902681-A1.	
XX		
PD	21-JAN-1999.	
XX		
PF	30-JUN-1998; 98MO-US13411.	
XX		
XX		
PR	24-JUL-1997; 97US-0899437.	
XX		
PR	09-JUL-1997; 97US-0052019.	
XX		
PA	(GETH) GENENTECH INC.	
XX		
PI	Godowski PJ, Matk MR, Zhang D;	
XX		
DR	WPI; 1999-120882/10.	
XX		
PT	New isolated neuroguilin related ligand-3 - used to develop products for treating nervous system disorders, e.g. stroke, Ischaemia,	

XX Claim 5(a): Page 69-70; 101pp: English.

CC This is the extracellular domain (ECD, aa1-360 of human neuregulin
CC related ligand NRG3 (see also AAM97618), a novel member of the
CC epidermal growth factor (EGF)-like family of protein ligands. NRG3
CC binds to the ErbB4 receptor, but not to the ErbB2 or ErbB3 receptor,
CC activates ErbB4 receptor tyrosine phosphorylation. The invention
CC provides human and murine polypeptides (see also AAM97617) that have
CC at least 75% homology to the NRG3 ECD, as well as expression vectors,
CC host cells and methods for the recombinant production of novel
CC NRG3s. The NRG3 polypeptides and polynucleotides and can be used to
CC enhance the survival, proliferation or differentiation of cells
CC having the ErbB4 receptor in vivo and in vitro. They can be used to
CC prevent or treat damage to a nerve or damage to other NRG3-expressing
CC or NRG3-responsive cells, e.g. brain, heart, or kidney cells. In
CC particular, they can be used to treat diseases which involve neural
CC cell growth such as demyelination, or damage or loss of glial cells
CC (e.g. multiple sclerosis). They can be used to treat patients whose
CC nervous system has been damaged by e.g. trauma, surgery, stroke,
CC ischemia, infection, metabolic disease, nutritional deficiency,
CC malignancy, or toxic agents. NRG3 can also be used to treat
CC motor neuron disorders such as amyotrophic lateral sclerosis (Lou
CC Gehrig's disease), Bell's palsy, conditions involving spinal
CC muscular atrophy or paralysis, neurodegenerative disorders such as
CC Alzheimer's disease, Parkinson's disease, epilepsy, multiple
CC sclerosis, Huntington's chorea, Down's syndrome, nerve deafness,
CC and Meniere's disease. They can also be used to treat neuropathies
CC associated with systemic disease including post-polio syndrome,
CC hereditary neuropathies including Charcot-Marie-Tooth disease,
CC Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC disease, metachromatic leukodystrophy, Fabry's disease and
CC Dejerine-Sottas syndrome, to treat disease of skeletal muscle of
CC smooth muscle, such as muscular dystrophy or diseases caused by
CC skeletal or smooth muscle wasting. The products can also be used
CC for detection, diagnosis, for the production of transgenic or
CC knockout animals or for drug screening.

XX Sequence 360 AA:

Query Match 100.0%; Score 277; DB 20; Length 360;
Best Local Similarity 100.0%; Pred. No. 1.1e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCDKDLAYCLNDGCEVFETLTGSHKRCRCKEGYGVRCDOPL 47
DB 286 hfkpcrkdlayclndgcefvletltgshkrcrckegygvrqdqfl 332

RESULT 4

AAM97620 standard; Protein; 362 AA.

XX AAM97620;

XX 10-MAY-1999 (first entry)

DE Mouse neuregulin related ligand NRG3 extracellular domain.

KW Neuregulin related ligand; NRG3; mouse; ErbB4 receptor;
KW signal transduction; nervous system disorder; neurodegeneration;
KW neuropathy; therapy; diagnosis.

XX Mus sp.

XX WO9902681-A1.

XX 21-JAN-1999.

XX 30-JUN-1998; 98WO-US13411.

XX 24-JUL-1997; 97US-0899437.

PR 09-JUL-1997; 97US-0052019.

XX (GETH) GENENTECH INC.

XX Godowski PJ, Mark MR, Zhang D;

XX WPI; 1999-120882/10.

PR New isolated neuregulin related ligand-3 - used to develop products
PR for treating nervous system disorders, e.g. stroke, ischemia,
PR infection, malignancy, Alzheimer's disease or Down's syndrome
XX Claim 5(a): Page 62-63; 101pp: English.

CC This is the extracellular domain (ECD, aa1-362) of murine neuregulin
CC related ligand NRG3 (see also AAM97617), a novel member of the
CC epidermal growth factor (EGF)-like family of protein ligands. NRG3
CC binds to the ErbB4 receptor, but not to the ErbB2 or ErbB3 receptor,
CC activates ErbB4 receptor tyrosine phosphorylation. The invention
CC provides human and murine polypeptides (see also AAM97618) that have
CC at least 75% homology to the NRG3 ECD, as well as expression vectors,
CC host cells and methods for the recombinant production of novel
CC NRG3s. The NRG3 polypeptides and polynucleotides and can be used to
CC enhance the survival, proliferation or differentiation of cells
CC having the ErbB4 receptor in vivo and in vitro. They can be used to
CC prevent or treat damage to a nerve or damage to other NRG3-expressing
CC or NRG3-responsive cells, e.g. brain, heart, or kidney cells. In
CC particular, they can be used to treat diseases which involve neural
CC cell growth such as demyelination, or damage or loss of glial cells
CC (e.g. multiple sclerosis). They can be used to treat patients whose
CC nervous system has been damaged by e.g. trauma, surgery, stroke,
CC ischemia, infection, metabolic disease, nutritional deficiency,
CC malignancy, or toxic agents. NRG3 can also be used to treat
CC motor neuron disorders such as amyotrophic lateral sclerosis (Lou
CC Gehrig's disease), Bell's palsy, conditions involving spinal
CC muscular atrophy or paralysis, neurodegenerative disorders such as
CC Alzheimer's disease, Parkinson's disease, epilepsy, multiple
CC sclerosis, Huntington's chorea, Down's syndrome, nerve deafness,
CC and Meniere's disease. They can also be used to treat neuropathies
CC associated with systemic disease including post-polio syndrome,
CC hereditary neuropathies including Charcot-Marie-Tooth disease,
CC Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC disease, metachromatic leukodystrophy, Fabry's disease and
CC Dejerine-Sottas syndrome, to treat disease of skeletal muscle of
CC smooth muscle, such as muscular dystrophy or diseases caused by
CC skeletal or smooth muscle wasting. The products can also be used
CC for detection, diagnosis, for the production of transgenic or
CC knockout animals or for drug screening.

XX Sequence 362 AA:

Query Match 100.0%; Score 277; DB 20; Length 362;
Best Local Similarity 100.0%; Pred. No. 1.1e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCDKDLAYCLNDGCEVFETLTGSHKRCRCKEGYGVRCDOPL 47
DB 288 hfkpcrkdlayclndgcefvletltgshkrcrckegygvrqdqfl 334

RESULT 5

AAM97619 standard; Protein; 696 AA.

XX AAM97619;

XX 10-MAY-1999 (first entry)

DE Human neuregulin related ligand NRG3 (splice variant).

KW Neuregulin related ligand; NRG3; hNRG3B1; human; ErbB4 receptor;
KW signal transduction; nervous system disorder; neurodegeneration;

XX	neuropathy; therapy; diagnosis; splice variant.
OS	Homo sapiens.
XH	
FH	Key
FT	Domain
FT	/note= "extracellular domain, specifically claimed in Claim 5(a)"
FT	Region
FT	/note= "hydrophobic region"
FT	66..91
FT	101..284
FT	/note= "mucln-like Ser/Thr-rich region, contains sites for O-linked glycosylation"
FT	Domain
FT	285..354
FT	/note= "EGF-like domain"
FT	356..394
FT	/note= "transmembrane domain"
FN	MO9902681-A1.
XX	
PD	21-JAN-1999.
PF	30-JUN-1998;
XX	98WO-US13411.
PR	24-JUL-1997;
PR	09-JUL-1997;
XX	97US-0899437.
PA	(GETH) GENENTECH INC.
PI	
PI	Godowski PJ, Mark MR, Zhang D;
DR	WPI: 1999-120882/10.
DR	N-PDB: AAX06989.
XX	
PT	New isolated neuroguilin related ligand-3 - used to develop products for treating nervous system disorders, e.g. stroke, ischemia, infection, malignancy, Alzheimer's disease or Down's syndrome
PS	Example 1; Page 78-81; 101pp; English.
XX	
CC	This is the amino acid sequence of splice variant hNGR3B2 of human neuroguilin related ligand NRG3, a novel member of the epidermal growth factor (EGF)-like family of protein ligands that binds to the ErbB4 receptor, but not to the ErbB2 or ErbB3 receptor, and which activates ErbB4 receptor tyrosine phosphorylation. The sequence was deduced from the nucleotide sequence of a cDNA clone (see AAX06989) from a foetal brain library. hNGR3B2 lacks amino acids 529-552 of hNGR3B1 (see AAU97618) but retains the EGF-like domain and is expected to exhibit biological activity. The invention provides human and murine NRG3 polypeptides (see AAU97617); expression vectors, host cells and methods for the recombinant production of NRG3s. The NRG3 polypeptides and polynucleotides can be used to enhance the survival, proliferation or differentiation of cells having the ErbB4 receptor in vivo and in vitro. They can be used to prevent or treat damage to a nerve or damage to other NRG3-expressing or NRG3-responsive cells, e.g. brain, heart, or kidney cells. In particular, they can be used to treat diseases which involve neural cell growth such as demyelination, or damage or loss of glial cells (e.g. multiple sclerosis). They can be used to treat patients whose nervous system has been damaged by e.g. trauma, surgery, stroke, ischemia, infection, metabolic disease, nutritional deficiency, malignancy, or toxic agents. NRG3 can also be used to treat motor neuron disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease), Bell's palsy, conditions involving spinal muscular atrophy or paralysis, neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's syndrome, nerve deafness, and Werner's disease. They can also be used to treat neuropathies associated with systemic disease including post-polio syndrome, hereditary neuropathies including Charcot-Marie-Tooth disease, Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's disease, metachromatic leukodystrophy, Fabry's disease and Dejerine-Sottas syndrome, to treat disease of skeletal muscle of

[illegible]

tyrosine phosphorylation. The sequence was deduced from the CC nucleotide sequences of cDNA clones (see AAX06987) from a mouse brain CC library. The EGF-like domain of NRG3 is distinct from those of NRG1 CC or NRG2, and NRG3 displays receptor binding characteristics that are CC distinct from those of other neuregulins. The invention provides CC human and murine NRG3 polypeptides (see also AAW97618), expression CC vectors, host cells and methods for the recombinant production of CC NRG3s. The NRG3 polypeptides and polynucleotides and can be used to CC enhance the survival, proliferation and differentiation of cells CC having the ErbB receptor in vivo and in vitro. They can be used to CC prevent or treat damage to a nerve or damage to other NRG3-expressing CC or NRG3-responsive cells, e.g. brain, heart, or kidney cells. In CC particular, they can be used to treat diseases which involve neural CC cell growth such as demyelination, or damage or loss of glial cells CC (e.g. multiple sclerosis). They can be used to treat patients whose CC nervous system has been damaged by e.g. trauma, surgery, stroke, CC ischemia, infection, metabolic disease, nutritional deficiency, CC malignancy, or toxic agents. NRG3 can also be used to treat CC motor neuron disorders such as amyotrophic lateral sclerosis (Lou CC Gehrig's disease), Bell's palsy, conditions involving spinal CC muscular atrophy or paralysis, neurodegenerative disorders such as CC Alzheimer's disease, Parkinson's disease, epilepsy, multiple CC sclerosis, Huntington's chorea, Down's syndrome, nerve deafness, CC and Meniere's disease. They can also be used to treat neuropathies CC associated with systemic disease including post-polio syndrome, CC hereditary neuropathies including Charcot-Marie-Tooth disease, CC Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's CC disease, metachromatic leukodystrophy, Fabry's disease and CC Dejerine-Sottas syndrome, to treat disease of skeletal muscle of CC smooth muscle, such as muscular dystrophy or diseases caused by CC skeletal or smooth muscle wasting. The products can also be used CC for detection, diagnosis, for the production of transgenic or CC knockout animals or for drug screening.

Sequence 713 AA:

Query Match 100.0%; Score 277; DB 20; Length 713;

Best Local Similarity 100.0%; Pred. No. 2e-20; Mismatches 0; Indels 0; Gaps 0;

Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

1 HFKPCRDKLAVCLNDGECFVETLTGSHKRCRKGYGVRCDQFL 47

288 hfkpcrdklavclndgecfvettltgshkrcrckegygvracdql 334

RESULT 7

AA05452 standard; Protein; 720 AA.

AA05452;

06-JUL-1999 (first entry)

Human heregulin-like factor sequence.

Human heregulin-like factor; HLF; cell growth regulator; diagnosis;

neural system disorder; cancer.

Homo sapiens.

WO9857989-A1.

23-DEC-1998.

16-JUN-1998; 98WO-US12403.

17-JUN-1997; 97US-0049942.

(HUMA-) HUMAN GENOME SCI INC.

(GEOU) UNIV GEORGETOWN.

Hijazi MM, King CR, Ruben SM, Young P;

WPI; 1999-095327/08.

New isolated heregulin-like factor - used to develop products for the diagnosis and treatment of disorders involving regulation of cell growth, particularly cancers

Disclosure; Page 97-99; 118pp; English.

This sequence is the human heregulin-like factor (HLF) of the CC invention. The HLF is involved in the regulation of cell growth. CC Detection of different levels of expression of the HLF gene can be used CC for the diagnosis of disorders, e.g. in the neural system. In CC particular, detection of different levels of HLF gene expression in cells CC or body fluid of an individual can be used for diagnosing cancer. The CC products can also be used in the treatment of disorders involving CC abnormal levels of HLF activity.

Sequence 720 AA:

Query Match 100.0%; Score 277; DB 20; Length 720;

Best Local Similarity 100.0%; Pred. No. 2.1e-20; Mismatches 0; Indels 0; Gaps 0;

Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

1 HFKPCRDKLAVCLNDGECFVETLTGSHKRCRKGYGVRCDQFL 47

286 hfkpcrdklavclndgecfvettltgshkrcrckegygvracdql 332

RESULT 8

AAW97618 standard; Protein; 720 AA.

AAW97618;

10-MAY-1999 (first entry)

Human neuregulin related ligand NRG3.

Neuregulin related ligand; NRG3; hNRG3B1; human; ErbB4 receptor;

signal transduction; nervous system disorder; neurodegeneration;

neuropathy; therapy; diagnosis.

Homo sapiens.

Location/Qualifiers

Domain

/note="extracellular domain, specifically claimed

in Claim 5(a)"

Region

/note="hydrophobic region"

Region

/note="mucin-like Ser/Thr-rich region, contains

sites for O-linked glycosylation"

Domain

/note="EGF-like domain"

/note="transmembrane domain"

WO9902681-A1.

21-JAN-1999.

30-JUN-1998; 98WO-US13411.

24-JUL-1997; 97US-0898437.

09-JUL-1997; 97US-0052019.

(GETH) GENENTECH INC.

Godowski PJ, Mark MR, Zhang D;

Sequence 52 AA;

```

QY 1 HFKPCRDKLAYCLNDGECFVIETLTGSHKH-CRCKEGYGVRCDOEL 47
    | | : : | | | : : | : : | | : :
Db 2 hlvcaeketlfcvngsecfmvkdlnpsrlylckcpgfsgarcqnyv 49

```

AC MAY69983

DT 20-APR-2000 (first entry)

NDF/heregulin protein family derivative peptide

balance disorder; therapy.

Synthetic.

PN US6017886-A

PD 25-JAN-2000

PF 23-FEB-1999; 99US-0255974.

PR : 05-AUG-1998; 98US-0129549.

(AMGE-) AMGEN INC.

PI Carnahan JF

DR WPI; 2000-136686/12.
XX

PT ear with a peptide, useful for treating hearing loss -

Claim 1; Fig 1; 11pp; English.

This sequence represents an *MBP*/herpulin protein family derivative peptide. The invention relates to a method for stimulating the proliferation of sensory epithelial cells of the inner ear, comprising contacting the cells with this sequence. The peptide acts as a growth factor to stimulate proliferation of cells in the sensory epithelium. The method is useful for the treatment of vestibular disorders (i.e., a balance disorder) or for treating hearing loss.

SQ	Sequence	52 AA;
1	1	1
2	2	2
3	3	3
4	4	4
5	5	5
6	6	6
7	7	7
8	8	8
9	9	9
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91	91	91
92	92	92
93	93	93
94	94	94
95	95	95
96	96	96
97	97	97
98	98	98
99	99	99
100	100	100

```
QY 1 HFKCRDKDLAYCLNDGECFVIETLTGSHKH-CRCKEGYGVRCDFL 477
   | | : : | | | : : | : : | : | : :
Db 2 hlvkcaeketfcvngsecfmykdlnsprylckcpgyfgarcqnyv 499
```

RESULT 12
AAW05184

AC AAW05184 ;

DT 04-JUN-1997 (first entry)

DE Neu differentiation factor/heréguin- α form EGF-like domain.
XY.

NDF: neu differentiation factor; heregulin; epidermal growth factor;
 EGF: colon epithelial cell proliferation; Schwann cell growth

KW	damage; colitis; ulcer
XX	

05
XX
SYNTHETIC.

PN W09031599-AL
XX

FD-10-OC1-1996
XX

FC 21 - MAR - 1990; 90WC-050426Z
XX

XX	2505-0417-040
XX	2505-0417-040

XX :
XX :

XX
XX

XX

XX stimulate proliferation of colon epithelial cells and Schwann cells
PT proteins - specifically from epidermal growth factor-like domain,
PT peptide(s) derived from new differentiation factor/herpangin
PT
PS Disclosures: Page 24, 37pp; English. ✓

CC The peptides AAW05182-W05185 are based on new differentiation factor
CC (NMN) domain14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29-30-31-32-33-34-35-36-37-38-39-40-41-42-43-44-45-46-47-48-49-50-51-52-53-54-55-56-57-58-59-60-61-62-63-64-65-66-67-68-69-70-71-72-73-74-75-76-77-78-79-80-81-82-83-84-85-86-87-88-89-90-91-92-93-94-95-96-97-98-99-100-101-102-103-104-105-106-107-108-109-110-111-112-113-114-115-116-117-118-119-120-121-122-123-124-125-126-127-128-129-130-131-132-133-134-135-136-137-138-139-140-141-142-143-144-145-146-147-148-149-150-151-152-153-154-155-156-157-158-159-160-161-162-163-164-165-166-167-168-169-170-171-172-173-174-175-176-177-178-179-180-181-182-183-184-185-186-187-188-189-190-191-192-193-194-195-196-197-198-199-200-201-202-203-204-205-206-207-208-209-210-211-212-213-214-215-216-217-218-219-220-221-222-223-224-225-226-227-228-229-230-231-232-233-234-235-236-237-238-239-240-241-242-243-244-245-246-247-248-249-250-251-252-253-254-255-256-257-258-259-260-261-262-263-264-265-266-267-268-269-270-271-272-273-274-275-276-277-278-279-280-281-282-283-284-285-286-287-288-289-290-291-292-293-294-295-296-297-298-299-300-301-302-303-304-305-306-307-308-309-310-311-312-313-314-315-316-317-318-319-320-321-322-323-324-325-326-327-328-329-330-331-332-333-334-335-336-337-338-339-340-341-342-343-344-345-346-347-348-349-350-351-352-353-354-355-356-357-358-359-360-361-362-363-364-365-366-367-368-369-370-371-372-373-374-375-376-377-378-379-380-381-382-383-384-385-386-387-388-389-390-391-392-393-394-395-396-397-398-399-400-401-402-403-404-405-406-407-408-409-410-411-412-413-414-415-416-417-418-419-420-421-422-423-424-425-426-427-428-429-430-431-432-433-434-435-436-437-438-439-440-441-442-443-444-445-446-447-448-449-450-451-452-453-454-455-456-457-458-459-460-461-462-463-464-465-466-467-468-469-470-471-472-473-474-475-476-477-478-479-480-481-482-483-484-485-486-487-488-489-490-491-492-493-494-495-496-497-498-499-500-501-502-503-504-505-506-507-508-509-510-511-512-513-514-515-516-517-518-519-520-521-522-523-524-525-526-527-528-529-530-531-532-533-534-535-536-537-538-539-540-541-542-543-544-545-546-547-548-549-550-551-552-553-554-555-556-557-558-559-560-561-562-563-564-565-566-567-568-569-570-571-572-573-574-575-576-577-578-579-580-581-582-583-584-585-586-587-588-589-590-591-592-593-594-595-596-597-598-599-600-601-602-603-604-605-606-607-608-609-610-611-612-613-614-615-616-617-618-619-620-621-622-623-624-625-626-627-628-629-630-631-632-633-634-635-636-637-638-639-640-641-642-643-644-645-646-647-648-649-650-651-652-653-654-655-656-657-658-659-660-661-662-663-664-665-666-667-668-669-670-671-672-673-674-675-676-677-678-679-680-681-682-683-684-685-686-687-688-689-690-691-692-693-694-695-696-697-698-699-700-701-702-703-704-705-706-707-708-709-710-711-712-713-714-715-716-717-718-719-720-721-722-723-724-725-726-727-728-729-730-731-732-733-734-735-736-737-738-739-740-741-742-743-744-745-746-747-748-749-750-751-752-753-754-755-756-757-758-759-760-761-762-763-764-765-766-767-768-769-770-771-772-773-774-775-776-777-778-779-780-781-782-783-784-785-786-787-788-789-790-791-792-793-794-795-796-797-798-799-800-801-802-803-804-805-806-807-808-809-810-811-812-813-814-815-816-817-818-819-820-821-822-823-824-825-826-827-828-829-830-831-832-833-834-835-836-837-838-839-840-841-842-843-844-845-846-847-848-849-850-851-852-853-854-855-856-857-858-859-860-861-862-863-864-865-866-867-868-869-870-871-872-873-874-875-876-877-878-879-880-881-882-883-884-885-886-887-888-889-890-891-892-893-894-895-896-897-898-899-900-901-902-903-904-905-906-907-908-909-910-911-912-913-914-915-916-917-918-919-920-921-922-923-924-925-926-927-928-929-930-931-932-933-934-935-936-937-938-939-940-941-942-943-944-945-946-947-948-949-950-951-952-953-954-955-956-957-958-959-960-961-962-963-964-965-966-967-968-969-970-971-972-973-974-975-976-977-978-979-980-981-982-983-984-985-986-987-988-989-990-991-992-993-994-995-996-997-998-999-1000-1001-1002-1003-1004-1005-1006-1007-1008-1009-1010-1011-1012-1013-1014-1015-1016-1017-1018-1019-1020-1021-1022-1023-1024-1025-1026-1027-1028-1029-1030-1031-1032-1033-1034-1035-1036-1037-1038-1039-1040-1

CC combinations. The peptides maintain the survival and proliferation of CC Schwann cells and cause no cell death.

colon epithelial cells. Accordingly, they are useful to treat (in vitro

ulcer) or of the nervous system (e.g. nerve damage caused by trauma).

50 Sequence 52 AA;

Query Match	41.08;	Score 113.5;	DB 17;	length 52;
Best Local Similarity	34.88;	Pred. No. 6.3e-05;		
Matches 16;	Conservative 14;	Mismatches 15;	Indels 1;	Gaps 1;

Dd 2 hlvkaeeketfcvnggecfmwkdlnpsrylckcpgyftgarcte. 47

RESULT 13

AA046918 standard; Protein; 63 AA.

AC AAR46918;
YY

DT	28-JUL-1994	(first entry)
YY		

DE	EGFL2.
KW	Glia1 growth factor; GGF; heregulin; mitogenesis;
KM	Schwann cell; tumour; central nervous system; erbB2 receptor;
KW	antiproliferative; epidermal growth factor; EGF.
XX	
PN	MO9403644-A.
XX	
PD	17-FEB-1994.
XX	
PF	10-AUG-1993; 93WO-US07491.
XX	
PR	10-AUG-1992; 92US-0927337.
PR	25-SEP-1992; 92US-0951747.
PR	01-DEC-1992; 92US-0984085.
PR	29-JAN-1993; 93US-0011396.
PA	(CAMP-) CAMBRIDGE NEUROSCIENCE INC.
XX	
PI	Gwynne DI, Marchionni M, McBurney RN;
XX	
DR	WPI: 1994-065731/08.
NR	N-PDB: AAO58324.
XX	
PT	Glia1 growth factor DNA encoding numerous polypeptide factors
PT	used for inhibiting cell proliferation - for treating carcinoma
PT	and nervous disorders
XX	
PS	Disclosure: Fig 40; 17pp; English.
CC	The GGF coding segments include regions with EGF-like homology.
CC	These EGF-like domains can be required for the activation of
CC	mitogenesis in the binding reaction between GGF ligands conty.
CC	such domains and the erbB2 receptor. Pref. antiproliferative
CC	factors are those which lack these EGF-like domains.
XX	
SQ	Sequence 63 AA;
OY	Query Match 41.0%; Score 113.5; DB 15; Length 63; Best Local Similarity 34.8%; Pred No. 7.5e-05; Matches 16; Conservative 14; Mismatches 15; Indels 1; Gaps 1;
DG	1 HERPGRNDLAYCLNDECEVETLTGSHKH-CRCKEYGVGVCDO 45 : : : : : : : : : 2 hlvcaeketfcvngcefwkdisnperylckcpgftgarcte 47
RESULT 14	
AAR55659	
ID	AAR55659 standard; Protein: 63 AA.
AC	AAR55659;
XX	
DDF	28-JUL-1994 (first entry)
XX	
DE	EGFL2.
XX	
KW	Glia1 growth factor; GGF; heregulin; mitogenesis;
KM	Schwann cell; tumour; central nervous system;
KW	epidermal growth factor; EGF.
XX	
PN	MO9400140-A.
XX	
PD	06-JAN-1994.
XX	
PF	29-JUN-1993; 93WO-US06228.
XX	
PR	30-JUN-1992; 92US-0907138.
PR	03-SEP-1992; 92US-0940388.
PR	23-OCT-1992; 92US-0965173.
PR	24-MAR-1993; 93US-0036555.
XX	

PA	(CMB-) CAMBRIDGE NEUROSCIENCE.
PA	(LUDW-) LUDWIG INST CANCER RES.
XX	
PI	Chen MS, Goodearl A, Hiles I, Marchionni M, Minnett L;
PI	Stroobant P, Waterfield M;
XX	
DR	WPI; 1994-025882/03.
XX	N-PSDB; AAQ62843.
PT	Glia1 mitogenic polypeptide factors - useful for stimulating
PT	glial cell mitogenesis and treating glial cell tumours
XX	
PS	Claim 53; Fig 39; 178pp: English.
XX	
CC	EGFL1, EGFL2, EGFL3, EGFL4, EGFL5 and EGFL6 are used
CC	for the stimulation of glial cell mitogenesis in vivo
CC	and in vitro.
XX	
SQ	Sequence 63 AA;
OY	Query Match 41.0%; Score 113.5; DB 15; Length 63; Best Local Similarity 34.8%; Pred. No. 7.5e-05; Matches 16; Conservative 14; Mismatches 15; Indels 1; Gaps 1;
DQ	1 HFKPRDKLAYCLNDGECEVETITGSHKH-CRCKEGYGVRCDQ 45 : : : : : : : : : 2 hlvkaeketkfcvngcefmwkdlnspyrickcpqpfgtgarc 47
DE	Homo sapiens.
KW	Epidermal like growth factor 2; mammalian muscle cell treatment;
KW	skeletal; cardiac; smooth; acetylcholine receptor deficiency;
KW	EGFL2.
OS	Homo sapiens.
PN	MO9426298-A.
PD	24-NOV-1994.
PE	06-MAY-1994; 94WO-0S05083.
PR	06-MAY-1993; 93US-0059022.
PR	08-MAR-1994; 94US-0209204.
FA	(CMB-) CAMBRIDGE NEUROSCIENCE.
PI	Gwynne DI, Marchionni M, Sklar R;
PI	WPI; 1995-006353/01.
DR	N-PSDB; AAQ74915.
PT	Treating mammalian muscle diseases and disorders - by admin. of
PT	Ggr2 and other specified polypeptide(s) which bind the p185erbB2
PT	receptor
XX	
XX	Claim 34; Pages 148-149; 241pp: English.
XX	AAQ74915 encodes AAR67250 human epidermal like growth factor 2 (EGFL2).
XX	The glial cell mitogenic activity of EGFL2 can be used to treat a
XX	variety of mammalian skeletal, cardiac and smooth muscle diseases,
XX	including acetylcholine receptor deficiency.

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OM protein - protein search, using sw model

Run on: February 7, 2002, 13:00:12 ; Search time 10.15:Seconds
(without alignments)
169.778 Million cell updates/sec

Title: US-09-480-977-4

Perfect score: 277

Sequence: 1 HRPCKRDLAVCLANDGECE.....SHKCRCKEGYGVRCQDFL 47

Scoring table:

BLOSUM62
Gapop 10.0, Gapext 0.5

Searched: 100059 seqs, 36664827 residues

Total number of hits satisfying chosen parameters: 100059

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database: SwissProt_39:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	277	100.0	713	1	NRG3_MOUSE
2	277	100.0	720	1	NRG3_HUMAN
3	126.5	45.7	677	1	NRG1_XENLA
4	113.5	41.0	639	1	NRG1_HUMAN
5	110	39.7	115	1	NRG4_MOUSE
6	104.5	37.7	236	1	SMDF_MOUSE
7	104	37.5	756	1	NRG2_HUMAN
8	102.5	37.0	662	1	NRG2_MOUSE
9	98.5	35.6	602	1	NRG1_CHICK
10	90	32.5	850	1	NRG2_HUMAN
11	90	32.5	868	1	NRG2_MOUSE
12	89.5	32.3	169	1	EREG_HUMAN
13	85	30.7	80	1	GREF_SEVKA
14	83	30.0	2531	1	NTC1_MOUSE
15	82.5	29.8	178	1	BTC_MOUSE
16	82.5	29.8	178	1	BTC_BOVIN
17	82	29.6	85	1	GREF_MTXVL
18	82	29.6	230	1	SPTC_HUMAN
19	80.5	28.7	142	1	GREF_VACCC
20	79.5	28.7	140	1	GREF_VACCC
21	79.5	28.7	142	1	GREF_VACCC
22	79.5	28.7	159	1	TGFA_MOUSE
23	79.5	28.7	159	1	TGFA_MOUSE
24	79	28.5	231	1	NTC1_MOUSE
25	78	28.2	1207	1	EGF_HUMAN
26	77.5	28.0	714	1	DLIL_MOUSE
27	77.5	28.0	722	1	DLIL_MOUSE
28	76	27.4	484	1	LEM2_PIG
29	76	27.4	1217	1	EGF_MOUSE
30	76	27.4	2139	1	GRB_DROME
31	75	27.1	611	1	LEM2_CANFA
32	74.5	26.9	603	1	FA12_CAVPO
33	74.5	26.9	723	1	DLIL_HUMAN

34	74.5	26.9	1429	1	LIL2_CAEEL	P14585 caenorhabd
35	74	26.7	551	1	LEM2_RABIT	P27113 oryctolagus
36	74	26.7	610	1	LEM2_HUMAN	P16381 homo sapien
37	74	26.7	2871	1	FBN1_BOVIN	P98133 bos taurus
38	74	26.7	2871	1	FBN1_HUMAN	P35555 homo sapien
39	74	26.7	2871	1	FBN1_MOUSE	O61554 mus musculu
40	74	26.7	2871	1	FBN1_PIG	O91336 sus scrofa
41	73	26.4	294	1	GRK_DROME	P42287 drosophila
42	73	26.4	409	1	MEGK_PIG	P79385 sus scrofa
43	73	26.4	1964	1	NTC4_MOUSE	P31695 mus musculu
44	73	26.4	2524	1	NTC4_XENLA	P21783 xenopus lae
45	72.5	26.2	121	1	TGFA_MACMU	P55244 macaca mula

ALIGNMENTS

RESULT 1
NRG3_MOUSE
ID NRG3_MOUSE STANDARD: PRT; 713 AA.
AC 035181:
DT 20-AUG-2001 (Rel. 40, Created)
DT 20-AUG-2001 (Rel. 40, Last sequence update)
DT 20-AUG-2001 (Rel. 40, Last annotation update)
DE PRO-NEUREGULIN-3 PRECURSOR (PRO-NRG3) [CONTAINS: NEUREGULIN-3 (NRG-3)].
DE NRG3.
GN Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=97420720; PubMed=9275162;
RA Zhang D., Sliwkowski M.X., Mark M., Frantz G., Akita R., Sun Y.,
RA Hillan K., Crowley C., Brush J., Godowski P.J.;
RT "Neuregulin-3 (NRG3): a novel neural tissue-enriched protein that
RT binds and activates ErbB4.";
RT Proc. Natl. Acad. Sci. U.S.A. 94:9562-9567(1997).
RL
CC - FUNCTION: DIRECT LIGAND FOR THE ERBB4 TYROSINE KINASE RECEPTOR.
CC - BINDING RESULTS IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND
CC ACTIVATION OF THE RECEPTOR. DOES NOT BIND TO THE EGF RECEPTOR.
CC - SUBCELLULAR LOCATION: EXISTS AS AN TYPE I MEMBRANE PROTEIN AND AS
CC A PROTOPLASMICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE
CC MEMBRANE-BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).
CC - TISSUE SPECIFICITY: EXPRESSED IN SYMPATHETIC, MOTOR, AND SENSORY
CC NEURONS.
CC - DEVELOPMENTAL STAGE: DETECTED AS EARLY AS E11. IN E13 EMBRYOS,
CC DETECTED MAINLY IN THE NERVOUS SYSTEM. IN E16 EMBRYOS, DETECTED IN
CC THE BRAIN, SPINAL CORD, TRIGEMINAL, VESTIBULAR-COCHLEAR, AND
CC SPINAL GANGLIA. IN ADULTS, EXPRESSED IN SPINAL CORD, AND NUMEROUS
CC BRAIN REGIONS.
CC - DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION
CC OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE
CC PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN
CC DIMERIZATION (BY SIMILARITY).
CC - DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE
CC DOMAIN (BY SIMILARITY).
CC - PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE
CC EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR
CC FORM (BY SIMILARITY).
CC - PTM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY
CC SIMILARITY).
CC - SIMILARITY: CONTRAINS 1 EGF-LIKE DOMAIN.
CC - SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.
CC
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CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. usage by and for commercial

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DR EMBL: AF010130; AAB70914.1; .
 DR MCD: MGT:1097165; NR93-like.
 DR InterPro: IPR000561; EGF-like.
 DR InterPro: IPR002154; Neuregulin.
 DR Pfam: PF00008; EGF; 1.
 DR Pfam: PF02158; Neuregulin; 1.
 DR SMART: SM00181; EGF; 1.
 DR PROSITE: PS00022; EGF-1; 1.
 DR PROSITE: PS01186; EGF-2; 1.
 DR Growth factor; EGF-like domain; Transmembrane; Multigene family.
 DR CHAIN 1 713 PRO-NEUREGULIN-3, MEMBRANE-BOUND FORM.
 FT CHAIN 1 361 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 1 362 INTERNAL SIGNAL SEQUENCE (POTENTIAL).
 FT DOMAIN 363 383 CYTOPLASMIC (POTENTIAL).
 FT DOMAIN 105 287 SER/THR-RICH.
 FT DOMAIN 288 331 EGF-LIKE.
 FT DOMAIN 13 21 POLY-ALA.
 FT DOMAIN 26 34 POLY-THR.
 FT DOMAIN 127 135 POLY-ALA.
 FT DOMAIN 250 253 POLY-SER.
 FT DOMAIN 254 263 POLY-SER.
 FT DISULFID 292 306 BY SIMILARITY.
 FT DISULFID 300 319 BY SIMILARITY.
 FT DISULFID 321 330 BY SIMILARITY.
 SO SEQUENCE 713 AA; 77369 MW; 9F7D1D5E7FC8DC60 CRC64;

Query Match 100.0%; Score 277; DB 1; Length 713;
 Best Local Similarity 100.0%; Pred. No. 6.2e-26;
 Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAYCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 47
 |||||
 DB 288 HFKPCRDKLAYCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 332

RESULT 2
 NR93_HUMAN STANDARD; PRT; 720 AA.
 AC P56975;
 DT 20-AUG-2001 (Rel. 40, Created)
 DT 20-AUG-2001 (Rel. 40, Last sequence update)
 DE 20-AUG-2001 (Rel. 40, Last annotation update)
 DE PRO-NEUREGULIN-3 PRECURSOR (PRO-NRG3) [CONTAINS: NEUREGULIN-3 (NRG-3)].
 GN NRG3.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE-Fetal brain;
 RX MEDLINE-97420720; PubMed-9275162;
 RA Zhang D., Sliwowski M.X., Frank G., Akita R., Sun Y., Hillman K., Crowley C., Bush J., Godowski P.J.;
 RA "Neuregulin-3 (NRG3): a novel neural tissue-enriched protein that binds and activates ErbB4.";
 RT Proc. Natl. Acad. Sci. U.S.A. 94:9562-9567(1997).
 CC -1- FUNCTION: DIRECT LIGAND FOR THE ERBB4 TYROSINE KINASE RECEPTOR. BINDING RESULTS IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND ACTIVATION OF THE RECEPTOR. DOES NOT BIND TO THE EGF RECEPTOR. ERBB2 OR ERBB3 RECEPTORS.
 CC -1- SUBCELLULAR LOCATION: EXISTS AS AN TYPE I MEMBRANE PROTEIN AND AS A PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE MEMBRANE-BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).
 CC -1- TISSUE SPECIFICITY: HIGHLY EXPRESSED IN MOST REGIONS OF THE BRAIN WITH THE EXCEPTION OF CORPUS CALLOSUM. EXPRESSED AT LOWER LEVEL IN

TESTIS. NOT DETECTED IN HEART, PLACENTA, LUNG, LIVER, SKELETAL MUSCLE, KIDNEY, PANCREAS, SPLEEN, THYMUS, PROSTATE, OVARY, SMALL INTESTINE, COLON AND PERIPHERAL BLOOD LEUKOCYTES.
 CC -1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE DIMERIZATION (BY SIMILARITY).
 CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE DOMAIN (BY SIMILARITY).
 CC -1- PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR FORM (BY SIMILARITY).
 CC -1- PTM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY SIMILARITY).
 CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
 CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.
 DR InterPro: IPR000561; EGF-like.
 DR InterPro: IPR002154; Neuregulin.
 DR Pfam: PF00008; EGF; 1.
 DR Pfam: PF02158; Neuregulin; 1.
 DR SMART: SM00181; EGF; 1.
 DR PROSITE: PS00022; EGF-1; 1.
 DR PROSITE: PS01186; EGF-2; 1.
 DR Growth factor; EGF-like domain; Transmembrane; Multigene family.
 DR CHAIN 1 720 PRO-NEUREGULIN-3, MEMBRANE-BOUND FORM.
 FT CHAIN 1 359 NEUREGULIN-3.
 FT TRANSMEM 361 381 EXTRACELLULAR (POTENTIAL).
 FT DOMAIN 382 720 INTERNAL SIGNAL SEQUENCE (POTENTIAL).
 FT DOMAIN 105 285 CYTOPLASMIC (POTENTIAL).
 FT DOMAIN 286 329 SER/THR-RICH.
 FT DOMAIN 5 8 EGF-LIKE.
 FT DOMAIN 13 21 POLY-ALA.
 FT DOMAIN 26 34 POLY-ALA.
 FT DOMAIN 127 135 POLY-THR.
 FT DOMAIN 252 260 POLY-SER.
 FT DOMAIN 262 265 POLY-SER.
 FT DISULFID 290 304 BY SIMILARITY.
 FT DISULFID 298 317 BY SIMILARITY.
 FT DISULFID 319 328 BY SIMILARITY.
 SO SEQUENCE 720 AA; 77900 MW; A4DEF10DD95A693 CRC64;

Query Match 100.0%; Score 277; DB 1; Length 720;
 Best Local Similarity 100.0%; Pred. No. 6.2e-26;
 Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 HFKPCRDKLAYCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 47
 |||||
 DB 286 HFKPCRDKLAYCLNDGECFVETLTGSHKCRCKEGYGVRCDOFL 332

RESULT 3
 NR91_XENLA STANDARD; PRT; 677 AA.
 AC O93383; Q9W6N0;
 DT 20-AUG-2001 (Rel. 40, Created)
 DT 20-AUG-2001 (Rel. 40, Last sequence update)
 DE 20-AUG-2001 (Rel. 40, Last annotation update)
 DE PRO-NEUREGULIN-1 PRECURSOR (PRO-NRG1) [CONTAINS: NEUREGULIN-1].
 GN NRG1.
 OS Xenopus laevis (African clawed frog).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidae; Pipidae;
 OC Xenopodinae; Xenopus.
 OX NCBI_TaxID=8355;
 RN [1]
 RP SEQUENCE FROM N.A. (ISOFORM ALPHA), AND ALTERNATIVE SPLICING. MEDLINE-98352126; PubMed-9685585;
 RA Yang J.F., Zhou H., Pun S., Ip N.Y., Peng H.B., Tsai K.W.K.;
 RA "Cloning of cDNAs encoding xenopus neuregulin: expression in myotomal muscle during embryo development.";
 RT Brain Res. Mol. Brain Res. 58:59-73(1998).

[21] SEQUENCE FROM N.A. (ISOFORM CRD).

RP MEDLINE-99316087; PubMed-10383827;

RA Yang J.F., Zhou H., Choi R.C., Ip N.Y., Peng H.B., Ts'ao K.W.K.;

RT A cytosolic-rich form of Xenopus neurogranin induces the expression of

RT acetylcholine receptors in cultured myotubes.;

RL Mol. Cell. Neurosci. 13:415-429(1999).

CC -1- FUNCTION: DIRECT LIGAND FOR THE ERBB TYROSINE KINASE RECEPTORS.

CC INDUCES EXPRESSION OF ACETYLCHOLINE RECEPTOR IN SYNAPTIC NUCLEI.

CC -1- SUBCELLULAR LOCATION: EXISTS AS A TYPE I MEMBRANE PROTEIN AND AS A

CC PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE MEMBRANE-

CC BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).

CC -1- ALTERNATIVE PRODUCTS: AT LEAST 2 ISOFORMS: ALPHA1 (SHOWN HERE) AND

CC CRD/CDNRG1 (CYSTEINE RICH DOMAIN); ARE PRODUCED BY ALTERNATIVE

CC SPLICING. ISOFORMS HAVE ALPHA OR BETA-TYPE EGF-LIKE DOMAINS.

CC -1- TISSUE SPECIFICITY: ISOFORM ALPHA1 IS EXPRESSED IN BRAIN AND

CC MUSCLE. ISOFORM CRD IS EXPRESSED IN BRAIN AND SPINAL CORD, BUT

CC AT VERY LOW LEVEL IN MUSCLE.

CC -1- DEVELOPMENTAL STAGE: STRONG EXPRESSION IN DEVELOPING BRAIN AND

CC SPINAL CORD OF THE EMBRYO. ALSO EXPRESSED IN THE MYOTOMAL MUSCLE.

CC -1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION

CC OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE

CC PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN

CC DIMERIZATION (BY SIMILARITY).

CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE

CC DOMAIN.

CC -1- PPM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE

CC EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR

CC FORM.

CC -1- PPM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY

CC SIMILARITY).

CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.

CC -1- SIMILARITY: CONTAINS 1 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAIN.

CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.

CC -----

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CC -----

DR EMBL; AF076618; AAC36804.1; -

DR EMBL; AF142632; AAD33893.1; -

DR HSSP; Q02297; IHRE.

DR InterPro; IPR000561; EGF-1like.

DR InterPro; IPR003006; IG_MHC.

DR InterPro; IPR003598; IG_C2.

DR InterPro; IPR002154; Neurogranin.

DR Pfam; PF00008; EGF; 1.

DR Pfam; PF00047; Ig; 1.

DR Pfam; PF02158; Neurogranin; 1.

DR PRINTS; PRO1089; NEUREGULIN.

DR SMART; SM00181; EGF; 1.

DR SMART; SM00408; IGC2; 1.

DR SMART; SM00408; IGC2; 1.

DR PROSITE; PS00022; EGF_1; 1.

DR PROSITE; PS01186; EGF_2; 1.

DR Growth factor; EGF-like domain; Immunoglobulin domain; Glycoprotein;

RV Transmembrane; Alternative splicing

FT CHAIN 1 259

FT CHAIN 1 677

FT DOMAIN 1 260

FT TRANSMEM 261 280

FT DOMAIN 281 677

FT DOMAIN 50 119

FT DOMAIN 188 232

FT DISULFID 57 116

FT DISULFID 192 206

FT DISULFID 200 220

FT DISULFID 222 231

FT DOMAIN 1 25

FT LYS-RICH.

FT PRO-NEUREGULIN ALPHA1 (BY SIMILARITY).

FT FORM (BY SIMILARITY).

FT EXTRACELLULAR (POTENTIAL).

FT INTERNAL SIGNAL SEQUENCE (POTENTIAL).

FT CYTOPLASMIC (POTENTIAL).

FT IG-LIKE C2-TYPE DOMAIN.

FT EGF-LIKE.

FT BY SIMILARITY.

FT BY SIMILARITY.

FT BY SIMILARITY.

FT BY SIMILARITY.

FT LYS-RICH.

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FT FT CARBOHYD 124 124 N-LINKED (GLCNAC... ) (POTENTIAL).
FT FT CARCHAND 130 130 N-LINKED (GLCNAC... ) (POTENTIAL).
FT FT VASPLIC 1 136 MAEKKAYREGGRGGRGGKKRDKRGKAESDDGNAASPRLKE
FT FT IKTOSVGEKTLVLTKQAVSPSLKFRMFKGEIKAKNK
FT FT PDSKRPHIKIRIGRKRSSELQISKASSADNGEKNVSNOJL
FT FT NDVTYVANTLYPK -> MSEDTAAGLQNCSESSPSPAE
FT FT LONESMPENDEDEETHGTIGTLCVCCEADRRLRCIN
FT FT SEKCIITPIIACLISLICIACTINGAKMWYDRKFEDSPHID
FT FT PGHHGDLILITDTAPSTLVVSVRTLVEIPPTDSKAAVT
FT FT FRFETSLDPE (IN ISOFORM CRD).
FT FT KCGTYARCFETDPLRVVRSEKHGIIEFME -> PNERTGD
FT FT RCNYVMASFVK (IN ISOFORM CRD).
FT FT SEQUENCE 677 AA; 75794 MW; 49279EB8FBAB3966f CRC64;
SQ

Query Match 45.7%; Score 126.5; DB 1; Length 677;
Best Local Similarity 43.5%; Pred. No. 6,4e-08;
Matches 20; Conservative 10; Mismatches 15; Indels 1; Gaps 1;

Oy 1 HKPRRDLDLAYCLNDGRCFYLETITSGHK-CRCKEYGYGRCO 45
Db 188 HLKSCDEKYTCVANGEGCYALNGITSSNOMPCRCRCPGTGARCTE 233

RESULT 4
NRG1_HUMAN STANDARD; PRT; 639 AA.
ID_NRG1_HUMAN Q02298; Q02298; Q12779; Q12780; Q12781; Q12782; Q12783;
AC AC Q12784; Q02298; Q02299; Q12780; Q12781; Q12782; Q12783;
AQ Q12784; Q02298; Q02299; Q12780; Q12781; Q12782; Q12783;
AT 20-AUG-2001 (Rel. 40, Created)
DT 20-AUG-2001 (Rel. 40, Last annotation update)
DT 20-AUG-2001 (Rel. 40, Last annotation update)
DE PRO-NEUREGULIN-1 PRECURSOR (PRO-NRG1) [CONTAINS: NEUREGULIN-1 (NEU
DE DIFFERENTIATION FACTOR) (HERESULIN) (HRG) (BREAST CANCER CELL
DE DIFFERENTIATION FACTOR P45) (ACEYLCHOLINE RECEPTOR INDUCING ACTIVITY)
DE (ARIA) (SENSORY AND MOTOR NEURON-DERIVED FACTOR) (GLIAL GROWTH
DE FACTOR)].
GN NRG1 OR HGL OR NDF OR HRGA OR GGF OR SHGF.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominiidae; Homo.
OC NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A. (ALPHA; BETA1; BETA2; BETA3), AND PARTIAL SEQUENCE.
RX MEDLINE=92271253; PubMed=1350381;
RA Holmes W.E., Siliwowski M.X., Akita R.W., Henzel W.J., Lee J.,
RA Park J.-Y., Yansura D., Abadi N., Raab H., Lewis G.D., Shepard H.M.,
RA Kuang W.-J., Wood W.I., Goeddel D.V., Vanden R.L.;
RT "Identification of heregulin, a specific activator of p185erbB2";
RL Science 236:1205-1210(1992).
RN [2]
RP SEQUENCE FROM N.A. (ALPHA2B; ALPHA3; BETA1A; BETA2 & BETA3).
RN [3]
RP TISSUE-Pituitary, and Kidney adenocarcinoma;
RX MEDLINE=94158863; PubMed=7509448;
RA Wen D., Sugis S.Y., Katunagaran D., Liu N., Cupples R.L., Luo Y.,
RA Janssen A.M., Ben-Baruch N., Trollinger D.B., Jacobsen V.L.,
RA Meng S.-Y., Lu H.S., Hu S., Chang D., Yang W., Yanigahara D.,
RA Koski R.A., Yarden Y.;
RT "Structural and functional aspects of the multiplicity of Neu
RT differential factors.";
RL Mol. Cell. Biol. 14:1909-1919(1994).
RN [4]
RP SEQUENCE FROM N.A. (ISOFORM ALPHA).
RX MEDLINE=92208945; PubMed=1348215;
RA Pales E., Bacus S.S., Koski R.A., Lu H.S., Wen D., Ogden S.G.,
RA Levy R.B., Yarden Y.;
RT "Isolation of the neu/her-2 stimulatory ligand: a 44 kd glycoprotein
RT that induces differentiation of mammary tumor cells";
RL Cell 69:205-216(1992).
RN [5]
RP SEQUENCE FROM N.A. (ISOFORMS BETA3 AND GGF2).
RX TISSUE-Brain;
RX MEDLINE=93205115; PubMed=8096067;

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PRINTS: PRO1089; NEUREGULIN.
DR PROSITE; PS00022; EGF_1; 1.
DR PROSITE; PS01186; EGF_2; 1.
DR Growth factor; EGF-like domain; Immunoglobulin domain; Glycoprotein;
KW Transmembrane; Multigene family; Polymorphism; 3D-structure;
KW Alternative splicing; Chromosomal translocation.
FT INIT_MER 0

Query Match 41.0%; Score 113.5; DB 1; Length 639;
Best Local Similarity 34.8%; Pred. No. 2.2e-06;
Matches 16; Conservative 14; Mismatches 15; Indels 1; Gaps 1;

OY 1 HKPCPKDVLAVCLNDGECFVETLTGSHKH-CRCKEGYGVRCQ 45
Db 177 HLYKCAKEKTECVNGGCEFWKDLNPSRYLCKCPGTFGARCTE 222

RESULT 5
NRG4_MOUSE STANDARD; PRT; 115 AA.
AC Q9WTX4;
DT 20-AUG-2001 (Rel. 40, Created)
DT 20-AUG-2001 (Rel. 40, Last sequence update)
DT 20-AUG-2001 (Rel. 40, Last annotation update)
DE PRO-NEUREGULIN-4, SHORT ISOFORM (PRO-NRG4) [CONTAINS: NEUREGULIN-4
(NRG-4)].
GN NRG4.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_Taxid=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=C57BL/6J; TISSUE=Liver;
RX MEDLINE=99276098; PubMed=10348342;
RA Hareel D., Tzahar E., Romano J., Shelly M., Pierce J.H., Andrews G.C.,
RA Yarden Y.;
RT "Neuregulin-4: a novel growth factor that acts through the ErbB-4
receptor tyrosine kinase."
RL Oncogene 18:2681-2689(1999).
CC -1- FUNCTION: LOW AFFINITY LIGAND FOR THE ERBB4 TYROSINE KINASE
RECEPTOR. CONCOMITANTLY RECRUITS ERBB1 AND ERBB2 CORECEPTORS,
RESULTING IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND
ACTIVATION OF THE ERBB RECEPTORS. DOES NOT BIND TO THE ERBB1,
ERBB2 AND ERBB3 RECEPTORS.
CC -1- SUBCELLULAR LOCATION: EXISTS AS AN TYPE I MEMBRANE PROTEIN AND AS
A PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE
MEMBRANE-BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).
CC -1- ALTERNATIVE PRODUCTS: AT LEAST 3 ISOFORMS MAY BE PRODUCED BY
ALTERNATIVE SPLICING.
CC -1- TISSUE SPECIFICITY: HIGHLY EXPRESSED IN PANCREAS; WEAKLY EXPRESSED
IN MUSCLE.
CC -1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION
OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE
PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN
DIMERIZATION (BY SIMILARITY).
CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE
DOMAIN (BY SIMILARITY).
CC -1- PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE
EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR
FORM (BY SIMILARITY).
CC -1- PTM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY
SIMILARITY).
CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.
CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.
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or send an email to license@isb-sib.ch).
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CC EMBL; AF083067; AAD21874.1;
DR InterPro; IPR000561; EGF-like.
DR InterPro; IPR001336; EGF_1.
DR Pfam; PF00008; EGF_1.
DR PRINTS; PRO0009; EGFTGF.
DR SMART; SM00181; EGF_1.
DR PROSITE; PS00022; EGF_1; 1.
DR PROSITE; PS01186; EGF_2; FALSE_NEG.
KW Growth factor; EGF-like domain; Glycoprotein; Transmembrane;
KW Multigene family; Alternative splicing.
FT CHAIN 1 115 PRO-NEUREGULIN-4, MEMBRANE-BOUND FORM.
FT CHAIN 1 61 NEUREGULIN-4.
FT DOMAIN 1 62 EXTRACELLULAR (POTENTIAL).
FT TRANSMEM 63 83 INTERNAL SIGNAL SEQUENCE (POTENTIAL).
FT DOMAIN 84 115 CYTOPLASMIC (POTENTIAL).
FT DOMAIN 5 46 EGF-LIKE.
FT DISULFID 9 23 BY SIMILARITY.
FT DISULFID 17 34 BY SIMILARITY.
FT DISULFID 36 45 BY SIMILARITY.
FT CARBOHYD 39 39 N-LINKED (GLCNAC...) (POTENTIAL).
FT CARBOHYD 60 60 N-LINKED (GLCNAC...) (POTENTIAL).
SQ SEQUENCE 115 AA; 12743 MW; 989A1B376857B49 CRC64;

Query Match 39.7%; Score 110; DB 1; Length 115;
Best Local Similarity 42.2%; Pred. No. 1.2e-06;
Matches 19; Conservative 8; Mismatches 16; Indels 2; Gaps 1;

OY 1 HKPCPKDVLAVCLNDGECFVETLTGSHKHCRCKEGYGVRCQ 45
Db 5 HEPGCGPRHRSECLNGICVITPTPS--PFCRCIENTYGANCEE 47

RESULT 6
SMDF_HUMAN STANDARD; PRT; 296 AA.
AC Q15491;
DT 20-AUG-2001 (Rel. 40, Created)
DT 20-AUG-2001 (Rel. 40, Last sequence update)
DT 20-AUG-2001 (Rel. 40, Last annotation update)
DE NEUREGULIN-1, SENSOR AND MOTOR NEURON-DERIVED FACTOR ISOFORM.
GN NRGI OR HGL OR NDF OR HRGA OR GGF OR SMDF.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.
OX NCBI_Taxid=9606;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain stem, and Cerebellum;
RX MEDLINE=95301541; PubMed=7782315;
RA Ho W.-H., Armanini M.P., Muijens A., Phillips H.S., Osherooff P.L.;
RT "Sensory and motor neuron-derived factor. A novel heregulin variant.
highly expressed in sensory and motor neurons."
RL J. Biol. Chem. 270:14523-14532(1995).
CC -1- FUNCTION: THE ISOFORM SMDF MAY PLAY A ROLE IN MOTOR AND SENSORY
NEURON DEVELOPMENT.
CC -1- SUBCELLULAR LOCATION: SECRETED. MAY POSSESS AN INTERNAL UNCLEAVED
SIGNAL SEQUENCE.
CC -1- ALTERNATIVE PRODUCTS: AT LEAST 10 ISOFORMS OF NRGI ARE PRODUCED BY
ALTERNATIVE SPLICING. EXCEPT FOR SMDF THEY ARE IN ENTRY AC 002397.
CC -1- TISSUE SPECIFICITY: EXPRESSED IN NERVOUS SYSTEM: SPINAL CORD MOTOR
NEURONS, DORSAL ROOT GANGLION NEURONS, AND BRAIN. PREDOMINANT
ISOFORM EXPRESSED IN SENSORY AND MOTOR NEURONS. NOT DETECTED IN
ADULT HEART, PLACENTA, LUNG, LIVER, SKELETAL MUSCLE, KIDNEY, AND
PANCREAS. NOT EXPRESSED IN FETAL LUNG, LIVER, AND KIDNEY.
CC -1- DEVELOPMENTAL STAGE: HIGHLY EXPRESSED IN DEVELOPING SPINAL MOTOR
NEURONS AND IN DEVELOPING CRANIAL NERVE NUCLEI. EXPRESSION IS
MAINTAINED ONLY IN BOTH ADULT MOTOR NEURONS AND DORSAL ROOT
GANGLION NEURONS.
CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.
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Db 249 HARKNETAKSYVNGCVCYIEGI--NQLSKCPGVGTGRCOOF 292

RESULT 8
 NRGI_RAT STANDARD; PRT: 662 AA.
 AC P43322; P43323; P43324; P43325; P43326; P43327; P43328;
 DT 20-AUG-2001 (Rel. 40, Created)
 DT 20-AUG-2001 (Rel. 40, Last sequence update)
 DT 20-AUG-2001 (Rel. 40, Last annotation update)
 DE PRO-NEUREGULIN-1 PRECURSOR (PRO-NRGI) (CONTAINS: NEUREGULIN-1 (NEU
 DE DIFFERENTIATION FACTOR) (HEREGULIN) (HRG) (ACETYLCHOLINE RECEPTOR
 DE INDUCING ACTIVITY) (ARIA) (SENSOR AND MOTOR NEURON-DERIVED FACTOR)
 DE (GLIAL GROWTH FACTOR)).
 GN NRGI OR NDF.
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_TaxID=10116;
 RN [1]
 RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
 RC TISSUE-Fibroblast; PubMed=7509448;
 RX MEDLINE=9415863; PubMed=7509448;
 RA Men D., Suggs S.V., Kartunagaran D., Liu N., Cupples R.L., Luo Y.,
 RA Janssen A.M., Ben-Baruch N., Trollinger D.B., Jacobsen V.L.,
 RA Meng S.-Y., Lu H.S., Hu S., Chang D., Yang W., Yanagihara D.,
 RA Koski R.A., Yarden Y.;
 RA Structural and functional aspects of the multiplicity of Neu
 RT differentiation factors.*;
 RL Mol. Cell. Biol. 14:1909-1919(1994).
 RN [2]
 RP SEQUENCE FROM N.A. (ISOFORM ALPHA2C/NDF44), AND PARTIAL SEQUENCE.
 RC TISSUE-Fibroblast;
 RX MEDLINE=92208945; PubMed=1348215;
 RA Men D., Peles E., Cupples R., Suggs S.V., Bacus S.S., Luo Y.,
 RA Traill G., Hu S., Slibiger S.M., Levy R.B., Koski R.A., Lu H.S.,
 RA Yarden Y.;
 RA New differentiation factor: a transmembrane glycoprotein containing
 RT an EGF domain and an immunoglobulin homology unit.*;
 RL Cell 69:559-572(1992).
 RN [3]
 RP SEQUENCE OF 14-36.
 RX MEDLINE=92208945; PubMed=1348215;
 RA Peles E., Bacus S.S., Koski R.A., Lu H.S., Men D., Ogden S.G.,
 RA Levy R.B., Yarden Y.;
 RA Isolation of the neu/HER-2 stimulatory ligand: a 44 kd glycoprotein
 RT that induces differentiation of mammary tumor cells.*;
 RL Cell 69:205-216(1992).
 RN [4]
 RP REGULATION OF PROCESSING (ISOFORM ALPHA2C/NDF44).
 RX MEDLINE=99069430; PubMed=9852099;
 RA Liu X., Huang H., Cao L., Men D., Liu N., Graham R.M., Zhou M.,
 RA Release of the neuregulin functional polypeptide requires its
 RT cytoplasmic tail.*;
 RL J. Biol. Chem. 273:34335-34340(1998).
 RN [5]
 RP INTERACTION WITH LIMK1.
 RX MEDLINE=98352096; PubMed=9685409;
 RA Wang J.Y., Frenzel K.E., Men D., Falls D.L.;
 RA Transmembrane neuregulins interact with Lim kinase 1, a cytoplasmic
 RT protein kinase implicated in development of visuospatial cognition.*;
 RL J. Biol. Chem. 273:20525-20534(1998).
 CC -1- FUNCTION: DIRECT LIGAND FOR ERBB3 AND ERBB4 TYROSINE KINASE
 CC RECEPTORS. CONCOMITANTLY RECRUITS ERBB1 AND ERBB2 CONCEPTORS,
 CC RESULTING IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND
 CC ACTIVATION OF THE ERBB RECEPTORS. THE MULTIPLE ISOFORMS PERFORM
 CC DIVERSE FUNCTIONS SUCH AS INDUCING GROWTH AND DIFFERENTIATION OF
 CC EPITHELIAL, GLIAL, NEURONAL, AND SKELETAL MUSCLE CELLS; INDUCING
 CC EXPRESSION OF ACETYLCHOLINE RECEPTOR IN SYNAPTIC VESICLES DURING
 CC LOBULOVULAR BUDDING AND MILK PRODUCTION IN THE MAMMARY GLAND
 CC AND INDUCING DIFFERENTIATION OF MAMMARY TUMOR CELLS; STIMULATING
 CC SCHWANN CELL PROLIFERATION; IMPLICATION IN THE DEVELOPMENT OF THE

CC MYOCARDIUM SUCH AS TRABECULATION OF THE DEVELOPING HEART (BY
 CC SIMILARITY).
 CC -1- SUBUNIT: THE CYTOPLASMIC DOMAIN INTERACTS WITH THE LIM DOMAIN
 CC REGION OF LIMK1.
 CC -1- SUBCELLULAR LOCATION: EXISTS AS A TYPE I MEMBRANE PROTEIN AND AS A
 CC PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE MEMBRANE-
 CC BOUND FORM DOES NOT SEEM TO BE ACTIVE.
 CC -1- ALTERNATIVE PRODUCTS: AT LEAST 8 ISOFORMS: ALPHA2A/NDF38,
 CC ALPHA2B/NDF19, ALPHA2C/NDF44, BETA1, BETA2/NDF40, BETA2A/NDF22,
 CC BETA3/NDF4 AND BETA4/NDF42A (SHOWN HERE); ARE PRODUCED BY
 CC ALTERNATIVE SPLICING.
 CC -1- TISSUE SPECIFICITY: WIDELY EXPRESSED. MOST TISSUES CONTAIN ALPHA2A
 CC AND ALPHA2B ISOFORMS. ALPHA2A AND BETA2 ARE THE PREDOMINANT FORMS
 CC IN MESENCHYMAL AND NONNEURONAL ORGANS. BETA1 IS ENRICHED IN BRAIN
 CC AND SPINAL CORD, BUT NOT IN MUSCLE AND HEART. ALPHA2C IS HIGHLY
 CC EXPRESSED IN SPINAL CORD, MODERATELY IN LUNG, BRAIN, OVARY, AND
 CC STOMACH, IN LOW AMOUNTS IN THE KIDNEY, SKIN AND PLACENTA.
 CC -1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION OF
 CC TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE
 CC PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN
 CC DIMERIZATION.
 CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE
 CC DOMAIN.
 CC -1- PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE
 CC EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR
 CC FORM.
 CC -1- PTM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE.
 CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
 CC -1- SIMILARITY: CONTAINS 1 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAIN.
 CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.
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 CC in the European Bioinformatics Institute. There are no restrictions on its
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 CC -----
 CC DR EMBL: U02315; AAA19940.1;
 CC DR EMBL: U02316; AAA19941.1;
 CC DR EMBL: U02317; AAA19942.1;
 CC DR EMBL: U02318; AAA19943.1;
 CC DR EMBL: U02319; AAA19944.1;
 CC DR EMBL: U02320; AAA19945.1;
 CC DR EMBL: U02321; AAA19946.1;
 CC DR EMBL: U02322; AAA19947.1;
 CC DR EMBL: U02323; AAA19948.1;
 CC DR EMBL: U02324; AAA19949.1;
 CC DR EMBL: M92430; -; NOT_ANNOTATED_CDS.
 CC DR HSPB: C02297; 1HRE.
 CC DR InterPro: IPR000561; EGF-Like.
 CC DR InterPro: IPR003006; Ig_MHC.
 CC DR InterPro: IPR003598; Ig_C2.
 CC DR InterPro: IPR002154; Neuregulin.
 CC DR Pfam: PF00008; EGF_1.
 CC DR Pfam: PF00047; Ig_1.
 CC DR Pfam: PF02158; Neuregulin; 1.
 CC DR PRINTS: SM01089; NEUREGULIN.
 CC DR SMART: SM00181; EGF; 1.
 CC DR SMART: SM00408; IGC2; 1.
 CC DR PROSITE: PS00022; EGF_1; 1.
 CC DR PROSITE: PS01186; EGF_2; FALSE NEG.
 CC KW Growth factor; EGF-like domain; Immunoglobulin domain; Glycoprotein;
 CC Transmembrane; Multigene family; Alternative splicing.
 CC FT PROPEP 1 13
 CC FT CHAIN 14 662 PRO-NEUREGULIN-1, MEMBRANE-BOUND FORM.
 CC FT CHAIN 14 264 NEUREGULIN-1.
 CC FT DOMAIN 14 265 EXTRACELLULAR (POTENTIAL).
 CC FT TRANSME 266 288 INTERNAL SIGNAL SEQUENCE (POTENTIAL).
 CC FT DOMAIN 289 662 CYTOPLASMIC (POTENTIAL).
 CC FT DOMAIN 50 119 IGF-LIKE C2-TYPE DOMAIN.

Query Match	Best Local Similarity	Score	DB 1	Length	662:
Matches 15; Conservative	31.28;	Pred. No. 4.7e-05;	Mismatches 13; Indels 1;	Gaps 1;	
1 HEPKCDKADLAVCLNDGCEFYETLTGSKRH-CRCKEAGYGRCDQFL 47					
178 HLIKCAKEKEKTEPCVNGGCECTYKDLSPNRSLCKCPNEFTGRCOMTV 225					
RESULT 9					
NRG1_CHICK	STANDARD:	PRT:	602 AA.		
AC 005199; 073750; 073751; 073752;					
DT 20-AUG-2001 (Rel. 40; Created)					
DT 20-AUG-2001 (Rel. 40; Last sequence update)					
DE 20-AUG-2001 (Rel. 40; Last annotation update)					
DE PRO-NEUREGULIN-1 PRECURSOR (PRO-NRG1) [CONTAINS: NEUREGULIN-1 (ACTEYLCHOLINE RECEPTOR INDUCING ACTIVITY) (ARIA)].					
DE NRG1 OR ARIA.					
OS Gallus gallus (Chicken).					
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;					
OC Archosauaria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;					
OC Gallus.					
OC NCBI_TaxID=9031;					
OX [1]					
RN SEQUENCE FROM N.A. (ISOFORM ARIA), AND PARTIAL SEQUENCE.					
RC STRAIN=WHITE LEGHORN; TISSUE=Brain;					
RA MEDLINE=93201602; PubMed=8453670;					
RA Falls D.L., Rosen K.M., Cortas G., Lane W.S., Fischbach G.D.;					
RT "ARIA, a protein that stimulates acetylcholine receptor synthesis, is					
RT a member of the neu ligand family.";					
RL Cell 72:801-815(1993).					
RN [2]					
RP SEQUENCE FROM N.A. (ISOFORMS BETA1A AND BETA2B).					
RC TISSUE=Brain, and Spinal cord;					
RA MEDLINE=98150951; PubMed=9491987;					
RA Yang X., Kuo Y., Devay P., Yu C., Role L.;					
RT "A cysteine-rich isoform of neuregulin controls the level of					
RT expression of neuronal nicotinic receptor channels during					
RT synaptogenesis.";					
RL Neuron 20:255-270(1996).					

CC -1- FUNCTION: DIRECT LIGAND FOR THE ERBB TYROSINE KINASE RECEPTORS.
CC THE MULTIPLE ISOFORMS PERFORM DIVERSE FUNCTIONS: CYSTEINE-RICH
CC DOMAIN CONTAINING ISOFORMS (CRD-NRG) PROBABLY REGULATE THE
CC EXPRESSION OF NICOTINIC ACETYLCHOLINE RECEPTORS AT DEVELOPING
CC INTERNEURONAL SYNAPSES. THE IG-NRG ISOFORM IS REQUIRED FOR THE
CC INITIAL INDUCTION AND/OR MAINTENANCE OF THE MATURE LEVELS OF
CC ACETYLCHOLINE RECEPTORS AT NEUROMUSCULAR SYNAPSES.
CC -1- SUBCELLULAR LOCATION: EXISTS AS A TYPE I MEMBRANE PROTEIN AND AS A
CC PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE MEMBRANE-
CC BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).
CC -1- ALTERNATIVE PRODUCTS: AT LEAST 4 ISOFORMS; ARV1/IG-NRG (SHOWN
CC HERE), CRD-NRG-BETA1A, CRD-NRG-BETA2A AND CRD-NRG-BETA2B; ARE
CC PRODUCED BY ALTERNATIVE SPLICING. ARIA CONTAINS AN IG-LIKE DOMAIN,
CC WHEREAS IN THE CRD-NRG (OR NARIA) ISOFORMS, THE EGF-LIKE DOMAIN IS
CC REPLACED BY A CYSTEINE-RICH DOMAIN (CRD).
CC -1- DEVELOPMENTAL STAGE: CRD-NRG ISOFORM IS DETECTED AT EMBRYONIC DAY
CC 4 (ED4) IN BOTH VISCERAL AND SOMATIC MOTOR NEURONS OF SPINAL CORD
CC AND IS HIGHEST AT ED6. IG-NRG ISOFORM IS NOT EXPRESSED UNTIL ED 6
CC IN SPINAL CORD. AT ED 11 BOTH ISOFORMS DISPLAY COMPARABLE LEVELS.
CC -1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION
CC OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE
CC PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN
CC DIMERIZATION (BY SIMILARITY).
CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE
CC DOMAIN.
CC -1- PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE
CC EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR
CC FORM.
CC -1- PTM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY
CC SIMILARITY).
CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
CC -1- SIMILARITY: CONTAINS 1 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAIN.
CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.

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CC or send an email to license@isb-sdb.ch).

CC EMBL, L11364; AAA49037.1; -
CC EMBL, AF045654; AAC05670.1; -
CC EMBL, AF045655; AAC05671.1; -
CC EMBL, AF045656; AAC05672.1; -
CC HSSP: Q02297; 1HRF.
CC InterPro: IPR000561; EGF-like.
CC InterPro: IPR003006; Ig_MHC.
CC InterPro: IPR003598; Ig_C2.
CC InterPro: IPR002154; Neuregulin.
CC Pfam: PF00047; Ig_1.
CC Pfam: PF02158; Neuregulin; 1.
CC PRINTS: PR01089; NEUREGULIN.
CC SMART: SM00181; EGF; 1.
CC SMART: SM00408; IgC2; 1.
CC PROSITE: PS00022; EGF_1; 1.
CC PROSITE: PS01186; EGF_2; FALSE_NEG.
CC Growth factor; EGF-like domain; Immunoglobulin domain; glycoprotein;
CC Transmembrane; Alternative splicing.
CC CHAIN 1 602 PRO-NEUREGULIN-1, MEMBRANE-BOUND FORM.
CC CHAIN 1 205 NEUREGULIN-1.
CC DOMAIN 1 206 EXTRACELLULAR (POTENTIAL).
CC TRANSMEM 207 229 INTERNAL SIGNAL SEQUENCE (POTENTIAL).
CC DOMAIN 230 602 CYTOPLASMIC (POTENTIAL).
CC DOMAIN 42 112 IG-LIKE C2-TYPE DOMAIN.
CC DOMAIN 125 136 SER/THR-RICH.
CC DOMAIN 137 181 EGF-LIKE.
CC DISULFID 49 105 BY SIMILARITY.
CC DISULFID 141 155 BY SIMILARITY.
CC DISULFID 149 169 BY SIMILARITY.
CC DISULFID 171 180 BY SIMILARITY.
CC CARBOHYD 21 21 N-LINKED (GLCNAC. .) (POTENTIAL).

FT CARBOHYD 113 113 N-LINKED (GLCNAC. . .) (POTENTIAL).
 FT CARBOHYD 126 126 N-LINKED (GLCNAC. . .) (POTENTIAL).
 FT VARSPLIC 1 127 MMTSECPLOYSLAPOTDWNSSYNTVPTKMKNOEVAV
 FT GOKLVLCETTSSEYPLAFKMLNKGKTEKKNKNOV
 FT KOKKSELIHYRATLADAGEACRVSCKLNDSTKSVIT
 FT DNNA -> MSENCTETPPSPSALSDASLGGCPAEENMG
 FT PHREDRSRVAVLSTCCVCLAEKRLKGLNCKICIAPI
 FT LACLSICLCTAGLKWVDFKIEYDSPHLDGRIQODPV
 FT STVDPTALSNMVEYVAFPIPSLESKAPVOTDSIV
 FT PSRPFLOPSLYNRIIDVGLSSATPSLSPSLEPTASAO
 FT ATEINLOTAPKLS (IN ISOFORM BETA1A, ISOFORM
 FT BETA2A AND ISOFORM BETA2B).
 FT MISSING (IN ISOFORM BETA2A AND ISOFORM
 FT BETA2B).
 FT VARSPLIC 191 198 VSAMTPPARNSPVDFHTP -> HTTPSTLLAGKSLRVS
 FT VARSPLIC 388 405 (IN ISOFORM BETA2B).
 FT VARSPLIC 406 602 MISSING (IN ISOFORM BETA2B).
 FT SEQUENCE 602 AA; 67453 MW; 4183C0B56CE5D346 CRC64;

Query Match 35.68; Score 98.5; DB 1; Length 602;
 Best Local Similarity 33.38; Pred. No. 0.00013;
 Matches 16; Conservative 11; Mismatches 20; Indels 1; Gaps 1;

OY 1 HEPFRNDKDLAYCLNDGCEPVITFLGSHKH-CRCKEGYGVGCDPL 47
 Db 137 HLRKCDIKAKAFVNGCEYVADLPNPRYLCRCNPEFGRCQNYV 184

RESULT 10
 NR02_HUMAN STANDARD; PRT; 850 AA.

AC 014511;
 DT 15-DEC-1998 (Rel. 37, Last sequence update)
 DT 20-AUG-2001 (Rel. 40, Last annotation update)
 DE PRO-NEUREGULIN-2 PRECURSOR (PRO-NRG2) [CONTAINS: NEUREGULIN-2 (NRG-2)
 DE (NEURAL-AND THYMUS-DERIVED ACTIVATOR FOR ERBB KINASES) (NTAK)
 DE (DERIVANT OF NEUREGULIN 1) (DON-1)].
 GN NRG2 OR NTAK.

OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.
 OX NCBI_TaxID=9606;

[1]
 RP SEQUENCE FROM N.A. (ISOFORM 1).

RC TISSUE=Neuroblastoma;
 RX MEDLINE=98006324; PubMed=9348101;
 RA Higashiyama S., Horikawa M., Yamada K., Ichino N., Nakano N.,
 RA Nakagawa T., Miyagawa J., Matsushita N., Nagatsu T., Taniguchi N.,
 RA Ishiguro H.;
 RA "A novel brain-derived member of the epidermal growth factor family
 that interacts with ErbB3 and ErbB4."
 RL J. Biochem. 122:675-680(1997).

[2]
 RP SEQUENCE FROM N.A. (ISOFORMS DON-1B AND DON-1R).

RC TISSUE=fetal brain;
 RX MEDLINE=97342638; PubMed=9199335;
 RA Woolf E.A., Michnick D.A., Chickerling T.W., Revett T.L., Ma J.,
 RA Woolf E.A., Comrick C.A., Dussault B.J., Woolf J., Goodearl A.D.J.,
 RA Geoling D.P.;
 RA "Characterization of a neuregulin-related gene, Don-1, that is highly
 RT expressed in restricted regions of the cerebellum and hippocampus."
 RL Mol. Cell. Biol. 17:4007-4014(1997).

[3]
 RP SEQUENCE FROM N.A. (ISOFORMS 1; 2; 3; 4; 5 AND 6).

RC TISSUE=Lung, and fetal brain;
 RX MEDLINE=99295836; PubMed=10369162;
 RA Rling H.Z., Chang H., Guillot A., Brice A., Leguero E., Francke U.;
 RA "The human neuregulin 2 (NRG2) gene: cloning, mapping and evaluation
 RT as a candidate for the autosomal recessive form of Charcot-Marie-Tooth
 RT disease linked to 5q."
 RL Hum. Genet. 104:326-332(1999).

CC -1- FUNCTION: DIRECT LIGAND FOR ERBB3 AND ERBB4 TYROSINE KINASE
 CC RECEPTORS. CONCOMITANTLY RECRUITS ERBB1 AND ERBB2 CORRECEPTORS,
 CC RESULTING IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND
 CC ACTIVATION OF THE ERBB RECEPTORS. MAY ALSO PROMOTE THE
 CC HETERODIMERIZATION WITH THE EGF RECEPTOR.
 CC -1- SUBCELLULAR LOCATION: EXISTS AS AN TYPE I MEMBRANE PROTEIN AND AS
 CC A PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE
 CC MEMBRANE-BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).
 CC -1- ALTERNATIVE PRODUCTS: 8 ISOFORMS; 1 (SHOWN HERE), 2, 3, 4, 5, 6,
 CC DON-1B AND DON-1R; ARE PRODUCED BY ALTERNATIVE SPLICING.
 CC -1- TISSUE SPECIFICITY: RESTRICTED TO THE CEREBELLUM IN THE ADULT.
 CC -1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION
 CC OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE
 CC PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN
 CC DIMERIZATION (BY SIMILARITY).
 CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE
 CC DOMAIN (BY SIMILARITY).
 CC -1- PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE
 CC EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR
 CC FORM (BY SIMILARITY).
 CC -1- PTM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY
 CC SIMILARITY).
 CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
 CC -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.

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DR EMBL: AB005060; BAA33417.1;
 DR EMBL: AF119162; AAF28848.1;
 DR EMBL: AF119151; AAF28848.1; JOINED.
 DR EMBL: AF119152; AAF28848.1; JOINED.
 DR EMBL: AF119153; AAF28848.1; JOINED.
 DR EMBL: AF119154; AAF28848.1; JOINED.
 DR EMBL: AF119155; AAF28848.1; JOINED.
 DR EMBL: AF119156; AAF28848.1; JOINED.
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 DR EMBL: AF119160; AAF28848.1; JOINED.
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 DR EMBL: AF119162; AAF28848.1; JOINED.
 DR EMBL: AF119151; AAF28848.1; JOINED.
 DR EMBL: AF119152; AAF28848.1; JOINED.
 DR EMBL: AF119153; AAF28848.1; JOINED.
 DR EMBL: AF119154; AAF28848.1; JOINED.
 DR EMBL: AF119155; AAF28848.1; JOINED.
 DR EMBL: AF119156; AAF28848.1; JOINED.
 DR EMBL: AF119157; AAF28848.1; JOINED.
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 DR EMBL: AF119160; AAF28848.1; JOINED.
 DR EMBL: AF119161; AAF28848.1; JOINED.
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 DR EMBL: AF119151; AAF28848.1; JOINED.
 DR EMBL: AF119152; AAF28848.1; JOINED.
 DR EMBL: AF119153; AAF28848.1; JOINED.
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 DR EMBL: AF119155; AAF28848.1; JOINED.
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 DR EMBL: AF119157; AAF28848.1; JOINED.
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 DR EMBL: AF119151; AAF28848.1; JOINED.
 DR EMBL: AF119152; AAF28848.1; JOINED.
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 DR EMBL: AF119155; AAF28848.1; JOINED.
 DR EMBL: AF119156; AAF28848.1; JOINED.
 DR EMBL: AF119157; AAF28848.1; JOINED.
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 DR EMBL: AF119151; AAF28848.1; JOINED.
 DR EMBL: AF119152; AAF28848.1; JOINED.
 DR EMBL: AF119153; AAF28848.1; JOINED.
 DR EMBL: AF119154; AAF28848.1; JOINED.
 DR EMBL: AF119155; AAF28848.1; JOINED.
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 DR E

PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN DIMERIZATION (BY SIMILARITY).
 -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE DOMAIN (BY SIMILARITY).
 -1- P.TM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR FORM (BY SIMILARITY).
 -1- P.TM: EXTENSIVE GLYCOSYLATION PRECEDES THE PROTEOLYTIC CLEAVAGE (BY SIMILARITY).
 -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
 -1- SIMILARITY: CONTAINS 1 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAIN.
 -1- SIMILARITY: BELONGS TO THE NEUREGULIN FAMILY.

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 EMBL: D89996; BAA23344.1; -
 EMBL: D89996; BAA23344.1; -
 EMBL: D89997; BAA23346.1; -
 EMBL: D89998; BAA23347.1; -
 EMBL: AB001576; BAA23348.1; -
 InterPro: IPR000561; EGF-like.
 InterPro: IPR003006; Ig_MHC.
 InterPro: IPR003598; Ig_C2.
 InterPro: IPR002154; Neuregulin.
 Pfam: PF00008; EGF; 1.
 Pfam: PF00047; Ig; 1.
 Pfam: PF02158; Neuregulin; 2.
 SMART: SM00181; EGF; 1.
 SMART: SM00408; IgC2; 1.
 PROSITE: PS00022; EGF_1; 1.
 PROSITE: PS01186; EGF_2; 1.
 Growth factor; EGF-like domain; Immunoglobulin domain; Glycoprotein; Transmembrane; Multigene family; Alternative splicing.
 PROPEP 1 127
 CHAIN 128 868
 CHAIN 128 428
 DOMAIN 128 429
 TRANSMEM 430 450
 DOMAIN 451 868
 DOMAIN 266 334
 DOMAIN 346 356
 DOMAIN 357 398
 DOMAIN 22 32
 DOMAIN 35 45
 DOMAIN 56 59
 DOMAIN 103 106
 DOMAIN 739 745
 DISULFID 273 327
 DISULFID 361 375
 DISULFID 369 386
 DISULFID 388 397
 CARBOHYD 33 33
 CARBOHYD 34 34
 CARBOHYD 163 163
 CARBOHYD 294 294
 CARBOHYD 362 362
 CARBOHYD 1 108
 VARSPLIC 220 222
 VARSPLIC 388 388
 VARSPLIC 389 868
 VARSPLIC 390 412
 VARSPLIC 390 421
 VARSPLIC 414 421
 VARSPLIC 414 439

FT VARSPLIC 440 868 SSSQSTSPSTLDN (IN ISOFORM NR02-ALPHA).
 FT CONFLICT 117 117 MISSING (IN ISOFORM NR02-ALPHA).
 FT CONFLICT 117 117 S -> F (IN REF. 2).
 FT CONFLICT 724 724 R -> H (IN REF. 2).
 SO SEQUENCE 868 AA; 93776 MW; 3C7D4D94DBE64DE2 CRC64;

 Query Match 32.5%; Score 90; DB 1; Length 868;
 Best Local Similarity 34.9%; Pred. No. 0.0019;
 Matches 15; Conservative 9; Mismatches 17; Indels 2; Caps 1;

 QY 1 HFKPCRDOLAYCLNGECPIVETLNSHHCRCKREYGVRC 43
 DB 357 HARKNETAKSTCVNGSVCIYIGI--NOLSCPKNGFQRC 397

 RESULT 12
 ID EREG_HUMAN STANDARD; PRT; 169 AA.
 AC 014944;
 DT 30-MAY-2000 (Rel. 39, Created)
 DT 30-MAY-2000 (Rel. 39, Last sequence update)
 DT 20-AUG-2001 (Rel. 40, Last annotation update)
 DE EPIREGULIN PRECURSOR.
 GN EREG.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
 OX NCBI_Taxid:9606;
 RN [1]
 RP SEQUENCE FROM N.A., AND CHARACTERIZATION.
 RC TISSUE-Colorectal adenocarcinoma;
 RX MEDLINE-97479200; PubMed-9337852;
 RA Toyoda H., Komurasaki T., Uchida D., Morimoto S.;
 RT Distribution of mRNA for human epieregulin, a differentially expressed member of the epidermal growth factor family.*;
 RL Biochem. J. 326:69-75(1997).
 CC -1- FUNCTION: MAY BE A MEDIATOR OF LOCALIZED CELL PROLIFERATION. AS A MITOGEN IT MAY STIMULATE CELL PROLIFERATION AND/OR ANGIOGENESIS.
 CC -1- SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN (PRECURSOR FORM); EXTRACELLULAR (MATURE FORM).
 CC -1- TISSUE SPECIFICITY: IN NORMAL ADULTS EXPRESSED PREDOMINANTLY IN THE IN CARCINOMAS OF THE BLADDER, LUNG, KIDNEY AND COLON.
 CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.

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 EMBL: D30783; BAA22146.1; -
 MIM: 602061;
 InterPro: IPR000561; EGF-like.
 InterPro: IPR001336; EGF_1.
 PRINTS: PRO0009; EGFGEF.
 SMART: SM00181; EGF; 1.
 PROSITE: PS01186; EGF_2; 1.
 Growth factor; Mitogen; Glycoprotein; EGF-like domain; Transmembrane; Signal.
 KW SIGNAL.
 FT SIGNAL 1 29
 FT PROPEP 30 59
 FT CHAIN 60 108
 FT PROPEP 109 169
 FT PROPEP 60 119
 FT TRANSMEM 120 140
 FT DOMAIN 141 169
 FT DOMAIN 145 152
 FT CARBOHYD 47 47
 FT DOMAIN 64 104
 EGF-LIKE.
 POTENTIAL.
 POTENTIAL.
 EPIREGULIN.
 REMOVED IN MATURE FORM (BY SIMILARITY).
 EXTRACELLULAR (POTENTIAL).
 POTENTIAL.
 CYTOPLASMIC (POTENTIAL).
 ARG/LYS-RICH (BASIC).
 N-LINKED (GLCNAC. . .) (POTENTIAL).
 EGF-LIKE.

FT	CHAIN	19	2531	NEUROGENIC LOCUS NOTCH HOMOLOG PROTEIN 1.
FT	DOMAIN	19	1723	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	1726	1746	POTENTIAL.
FT	DOMAIN	1747	2531	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	20	58	EGF-LIKE 1.
FT	DOMAIN	59	99	EGF-LIKE 2.
FT	DOMAIN	102	139	EGF-LIKE 3.
FT	DOMAIN	140	176	EGF-LIKE 4.
FT	DOMAIN	178	216	EGF-LIKE 5.
FT	DOMAIN	218	255	EGF-LIKE 6.
FT	DOMAIN	257	293	EGF-LIKE 7.
FT	DOMAIN	295	333	EGF-LIKE 8.
FT	DOMAIN	335	371	EGF-LIKE 9.
FT	DOMAIN	372	410	EGF-LIKE 10.
FT	DOMAIN	412	450	EGF-LIKE 11.
FT	DOMAIN	452	488	EGF-LIKE 12.
FT	DOMAIN	490	526	EGF-LIKE 13.
FT	DOMAIN	528	564	EGF-LIKE 14.
FT	DOMAIN	566	601	EGF-LIKE 15.
FT	DOMAIN	603	639	EGF-LIKE 16.
FT	DOMAIN	641	676	EGF-LIKE 17.
FT	DOMAIN	678	714	EGF-LIKE 18.
FT	DOMAIN	716	751	EGF-LIKE 19.
FT	DOMAIN	753	789	EGF-LIKE 20.
FT	DOMAIN	791	827	EGF-LIKE 21.
FT	DOMAIN	829	867	EGF-LIKE 22.
FT	DOMAIN	869	905	EGF-LIKE 23.
FT	DOMAIN	907	943	EGF-LIKE 24.
FT	DOMAIN	945	981	EGF-LIKE 25.
FT	DOMAIN	983	1019	EGF-LIKE 26.
FT	DOMAIN	1021	1057	EGF-LIKE 27.
FT	DOMAIN	1059	1095	EGF-LIKE 28.
FT	DOMAIN	1097	1143	EGF-LIKE 29.
FT	DOMAIN	1145	1181	EGF-LIKE 30.
FT	DOMAIN	1183	1219	EGF-LIKE 31.
FT	DOMAIN	1221	1265	EGF-LIKE 32.
FT	DOMAIN	1267	1305	EGF-LIKE 33.
FT	DOMAIN	1307	1346	EGF-LIKE 34.
FT	DOMAIN	1348	1384	EGF-LIKE 35.
FT	DOMAIN	1387	1426	EGF-LIKE 36.
FT	DOMAIN	1449	1462	CYS-RICH.
FT	REPEAT	1445	1480	EGF-LIKE 37.
FT	REPEAT	1481	1522	EGF-LIKE 38.
FT	REPEAT	1523	1562	EGF-LIKE 39.
FT	REPEAT	1563	1601	EGF-LIKE 40.
FT	REPEAT	1602	1641	EGF-LIKE 41.
FT	REPEAT	1642	1681	EGF-LIKE 42.
FT	REPEAT	1682	1721	EGF-LIKE 43.
FT	REPEAT	1722	1761	EGF-LIKE 44.
FT	REPEAT	1762	1801	EGF-LIKE 45.
FT	REPEAT	1802	1841	EGF-LIKE 46.
FT	REPEAT	1842	1881	EGF-LIKE 47.
FT	REPEAT	1882	1921	EGF-LIKE 48.
FT	REPEAT	1922	1961	EGF-LIKE 49.
FT	REPEAT	1962	2001	EGF-LIKE 50.
FT	REPEAT	2002	2041	EGF-LIKE 51.
FT	REPEAT	2042	2081	EGF-LIKE 52.
FT	REPEAT	2082	2121	EGF-LIKE 53.
FT	REPEAT	2122	2161	EGF-LIKE 54.
FT	REPEAT	2162	2201	EGF-LIKE 55.
FT	REPEAT	2202	2241	EGF-LIKE 56.
FT	REPEAT	2242	2281	EGF-LIKE 57.
FT	REPEAT	2282	2321	EGF-LIKE 58.
FT	REPEAT	2322	2361	EGF-LIKE 59.
FT	REPEAT	2362	2401	EGF-LIKE 60.
FT	REPEAT	2402	2441	EGF-LIKE 61.
FT	REPEAT	2442	2481	EGF-LIKE 62.
FT	REPEAT	2482	2521	EGF-LIKE 63.
FT	REPEAT	2522	2561	EGF-LIKE 64.
FT	REPEAT	2562	2601	EGF-LIKE 65.
FT	REPEAT	2602	2641	EGF-LIKE 66.
FT	REPEAT	2642	2681	EGF-LIKE 67.
FT	REPEAT	2682	2721	EGF-LIKE 68.
FT	REPEAT	2722	2761	EGF-LIKE 69.
FT	REPEAT	2762	2801	EGF-LIKE 70.
FT	REPEAT	2802	2841	EGF-LIKE 71.
FT	REPEAT	2842	2881	EGF-LIKE 72.
FT	REPEAT	2882	2921	EGF-LIKE 73.
FT	REPEAT	2922	2961	EGF-LIKE 74.
FT	REPEAT	2962	3001	EGF-LIKE 75.
FT	REPEAT	3002	3041	EGF-LIKE 76.
FT	REPEAT	3042	3081	EGF-LIKE 77.
FT	REPEAT	3082	3121	EGF-LIKE 78.
FT	REPEAT	3122	3161	EGF-LIKE 79.
FT	REPEAT	3162	3201	EGF-LIKE 80.
FT	REPEAT	3202	3241	EGF-LIKE 81.
FT	REPEAT	3242	3281	EGF-LIKE 82.
FT	REPEAT	3282	3321	EGF-LIKE 83.
FT	REPEAT	3322	3361	EGF-LIKE 84.
FT	REPEAT	3362	3401	EGF-LIKE 85.
FT	REPEAT	3402	3441	EGF-LIKE 86.
FT	REPEAT	3442	3481	EGF-LIKE 87.
FT	REPEAT	3482	3521	EGF-LIKE 88.
FT	REPEAT	3522	3561	EGF-LIKE 89.
FT	REPEAT	3562	3601	EGF-LIKE 90.
FT	REPEAT	3602	3641	EGF-LIKE 91.
FT	REPEAT	3642	3681	EGF-LIKE 92.
FT	REPEAT	3682	3721	EGF-LIKE 93.
FT	REPEAT	3722	3761	EGF-LIKE 94.
FT	REPEAT	3762	3801	EGF-LIKE 95.
FT	REPEAT	3802	3841	EGF-LIKE 96.
FT	REPEAT	3842	3881	EGF-LIKE 97.
FT	REPEAT	3882	3921	EGF-LIKE 98.
FT	REPEAT	3922	3961	EGF-LIKE 99.
FT	REPEAT	3962	4001	EGF-LIKE 100.
FT	REPEAT	4002	4041	EGF-LIKE 101.
FT	REPEAT	4042	4081	EGF-LIKE 102.
FT	REPEAT	4082	4121	EGF-LIKE 103.
FT	REPEAT	4122	4161	EGF-LIKE 104.
FT	REPEAT	4162	4201	EGF-LIKE 105.
FT	REPEAT	4202	4241	EGF-LIKE 106.
FT	REPEAT	4242	4281	EGF-LIKE 107.
FT	REPEAT	4282	4321	EGF-LIKE 108.
FT	REPEAT	4322	4361	EGF-LIKE 109.
FT	REPEAT	4362	4401	EGF-LIKE 110.
FT	REPEAT	4402	4441	EGF-LIKE 111.
FT	REPEAT	4442	4481	EGF-LIKE 112.
FT	REPEAT	4482	4521	EGF-LIKE 113.
FT	REPEAT	4522	4561	EGF-LIKE 114.
FT	REPEAT	4562	4601	EGF-LIKE 115.
FT	REPEAT	4602	4641	EGF-LIKE 116.
FT	REPEAT	4642	4681	EGF-LIKE 117.
FT	REPEAT	4682	4721	EGF-LIKE 118.
FT	REPEAT	4722	4761	EGF-LIKE 119.
FT	REPEAT	4762	4801	EGF-LIKE 120.
FT	REPEAT	4802	4841	EGF-LIKE 121.
FT	REPEAT	4842	4881	EGF-LIKE 122.
FT	REPEAT	4882	4921	EGF-LIKE 123.
FT	REPEAT	4922	4961	EGF-LIKE 124.
FT	REPEAT	4962	5001	EGF-LIKE 125.
FT	REPEAT	5002	5041	EGF-LIKE 126.
FT	REPEAT	5042	5081	EGF-LIKE 127.
FT	REPEAT	5082	5121	EGF-LIKE 128.
FT	REPEAT	5122	5161	EGF-LIKE 129.
FT	REPEAT	5162	5201	EGF-LIKE 130.
FT	REPEAT	5202	5241	EGF-LIKE 131.
FT	REPEAT	5242	5281	EGF-LIKE 132.
FT	REPEAT	5282	5321	EGF-LIKE 133.
FT	REPEAT	5322	5361	EGF-LIKE 134.
FT	REPEAT	5362	5401	EGF-LIKE 135.
FT	REPEAT	5402	5441	EGF-LIKE 136.
FT	REPEAT	5442	5481	EGF-LIKE 137.
FT	REPEAT	5482	5521	EGF-LIKE 138.
FT	REPEAT	5522	5561	EGF-LIKE 139.
FT	REPEAT	5562	5601	EGF-LIKE 140.
FT	REPEAT	5602	5641	EGF-LIKE 141.
FT	REPEAT	5642	5681	EGF-LIKE 142.
FT	REPEAT	5682	5721	EGF-LIKE 143.
FT	REPEAT	5722	5761	EGF-LIKE 144.
FT	REPEAT	5762	5801	EGF-LIKE 145.
FT	REPEAT	5802	5841	EGF-LIKE 146.
FT	REPEAT	5842	5881	EGF-LIKE 147.
FT	REPEAT	5882	5921	EGF-LIKE 148.
FT	REPEAT	5922	5961	EGF-LIKE 149.
FT	REPEAT	5962	6001	EGF-LIKE 150.
FT	REPEAT	6002	6041	EGF-LIKE 151.
FT	REPEAT	6042	6081	EGF-LIKE 152.
FT	REPEAT	6082	6121	EGF-LIKE 153.
FT	REPEAT	6122	6161	EGF-LIKE 154.
FT	REPEAT	6162	6201	EGF-LIKE 155.
FT	REPEAT	6202	6241	EGF-LIKE 156.
FT	REPEAT	6242	6281	EGF-LIKE 157.
FT	REPEAT	6282	6321	EGF-LIKE 158.
FT	REPEAT	6322	6361	EGF-LIKE 159.
FT	REPEAT	6362	6401	EGF-LIKE 160.
FT	REPEAT	6402	6441	EGF-LIKE 161.
FT	REPEAT	6442	6481	EGF-LIKE 162.
FT	REPEAT	6482	6521	EGF-LIKE 163.
FT	REPEAT	6522	6561	EGF-LIKE 164.
FT	REPEAT	6562	6601	EGF-LIKE 165.
FT	REPEAT	6602	6641	EGF-LIKE 166.
FT	REPEAT	6642	6681	EGF-LIKE 167.
FT	REPEAT	6682	6721	EGF-LIKE 168.
FT	REPEAT	6722	6761	EGF-LIKE 169.
FT	REPEAT	6762	6801	EGF-LIKE 170.
FT	REPEAT	6802	6841	EGF-LIKE 171.
FT	REPEAT	6842	6881	EGF-LIKE 172.
FT	REPEAT	6882	6921	EGF-LIKE 173.
FT	REPEAT	6922	6961	EGF-LIKE 174.
FT	REPEAT	6962	7001	EGF-LIKE 175.
FT	REPEAT	7002	7041	EGF-LIKE 176.
FT	REPEAT	7042	7081	EGF-LIKE 177.
FT	REPEAT	7082	7121	EGF-LIKE 178.
FT	REPEAT	7122	7161	EGF-LIKE 179.
FT	REPEAT	7162	7201	EGF-LIKE 180.
FT	REPEAT	7202	7241	EGF-LIKE 181.
FT	REPEAT	7242	7281	EGF-LIKE 182.
FT	REPEAT	7282	7321	EGF-LIKE 183.
FT	REPEAT	7322	7361	EGF-LIKE 184.
FT	REPEAT	7362	7401	EGF-LIKE 185.
FT	REPEAT	7402	7441	EGF-LIKE 186.
FT	REPEAT	7442	7481	EGF-LIKE 187.
FT	REPEAT	7482	7521	EGF-LIKE 188.
FT	REPEAT	7522	7561	EGF-LIKE 189.
FT	REPEAT	7562	7601	EGF-LIKE 190.
FT	REPEAT	7602	7641	EGF-LIKE 191.
FT	REPEAT	7642	7681	EGF-LIKE 192.
FT	REPEAT	7682	7721	EGF-LIKE 193.
FT	REPEAT	7722	7761	EGF-LIKE 194.
FT	REPEAT	7762	7801	EGF-LIKE 195.
FT	REPEAT	7802	7841	EGF-LIKE 196.
FT	REPEAT	7842	7881	EGF-LIKE 197.
FT	REPEAT	7882	7921	EGF-LIKE 198.
FT	REPEAT	7922	7961	EGF-LIKE 199.
FT	REPEAT	7962	8001	EGF-LIKE 200.
FT	REPEAT	8002	8041	EGF-LIKE 201.
FT	REPEAT	8042	8081	EGF-LIKE 202.
FT	REPEAT	8082	8121	EGF-LIKE 203.
FT	REPEAT	8122	8161	EGF-LIKE 204.
FT	REPEAT	8162	8201	EGF-LIKE 205.
FT	REPEAT	8202	8241	EGF-LIKE 206.
FT	REPEAT	8242	8281	EGF-LIKE 207.
FT	REPEAT	8282	8321	EGF-LIKE 208.
FT	REPEAT	8322	8361	EGF-LIKE 209.
FT	REPEAT	8362	8401	EGF-LIKE 210.
FT	REPEAT	8402	8441	EGF-LIKE 211.
FT	REPEAT	8442	8481	EGF-LIKE 212.
FT	REPEAT	8482	8521	EGF-LIKE 213.
FT	REPEAT	8522	8561	EGF-LIKE 214.
FT	REPEAT	8562	8601	EGF-LIKE 215.
FT	REPEAT	8602	8641	EGF-LIKE 216.
FT	REPEAT	8642	8681	EGF

Search completed: February 7, 2002, 13:03:16
Job time: 184 sec

GN BTC OR BCN.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A., AND SEQUENCE OF 32-54; 64-71 AND 75-111.
RC TISSUE=Pancreas;
RX MEDLINE=93206093; PubMed=8456283;
RA Shing Y., Christofori G., Hanahan D., Ono Y., Sasada R.,
RA Igarashi K., Folkman J.;
RT "Betacellulin: a mitogen from pancreatic beta cell tumors.";
RL Science 259:1604-1607(1993).
CC -1- FUNCTION: POTENT MITOGEN FOR RETINAL PIGMENT EPITHELIAL CELLS
CC AND VASCULAR SMOOTH MUSCLE CELLS. THE EFFECTS OF BETACELLULIN
CC ARE PROBABLY MEDIATED BY THE EGF RECEPTOR AND OTHER RELATED
CC RECEPTORS.
CC -1- SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN (PRECURSOR FORM);
CC EXTRACELLULAR (MATURE FORM).
CC -1- TISSUE SPECIFICITY: FOUND IN SEVERAL MOUSE TISSUES INCLUDING
CC KIDNEY, UTERUS AND LIVER AS WELL AS IN BETA TUMOR CELL LINE AND
CC MCF-7 CELLS. IT IS NOT DETECTED IN THE BRAIN.
CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
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CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).
CC -----
CC EMBL: L08394; AAA0511.1; -
DR PIR: A37408; A37408.
DR HSSP: P01135; 1YUF.
DR MCD: MCI:99439; BTC.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR001336; EGF_1.
DR Pfam: PF00008; EGF; 1.
DR PRINTS: PRO0009; EGF_TGF.
DR SMART: SM00181; EGF; 1.
DR SMART: SM00001; EGF-like; 1.
DR PROSITE: PS00022; EGF_1; 1.
DR PROSITE: PS01186; EGF_2; 1.
DR Growth factor; Mitogen; Glycoprotein; EGF-like domain; Transmembrane;
KW Signal.
FT SIGNAL. 1 31
FT CHAIN. 32 111
FT PROPEP. 112 177
FT DOMAIN. 32 118
FT TRANSMEM. 119 139
FT DOMAIN. 140 177
FT DOMAIN. 65 105
FT DOMAIN. 146 153
FT DISULFID. 69 82
FT DISULFID. 77 93
FT DISULFID. 95 104
FT CARBOHYD. 34 34
FT CARBOHYD. 42 42
FT CARBOHYD. 52 52
SQ SEQUENCE. 177 AA; 19664 MW; 066B34F0E13F82B CRC64;

Query Match 29.8%; Score 82.5; DB 1; Length 177;
Best Local Similarity 39.1%; Pred. No. 0.0035;
Matches 18; Conservative 9; Mismatches 14; Indels 5; Gaps 3;

OY 1 HFPCRDRLAYGLNDEEC-FVLETGSHKCKCKESYGVCRCQ 45
Db 65 HFSRCPKYKHYCIH-GRCRFVVDQTPS---CICGKYGFCRCR 106

GenCore version 4.5
Copyright (c) 1993 - 2000 Compugen Ltd.

OM protein - protein search, using sw model

Run on: February 7, 2002, 12:59:52 Search time 22.8 Seconds
(without alignments)
301.526 Million cell updates/sec

Title: US-09-480-977-4

Sequence: 1 HRPCKRDNDLAYCLNDGECF.....SHKHCKCKGKGVGRCDQFL 47

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 473505 seqs, 146272329 residues

Total number of hits satisfying chosen parameters: 473505

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

- Database:
- 1: SPREMBL_17:*
 - 2: sp.archaea:*
 - 3: sp.bacteria:*
 - 4: sp.fungi:*
 - 5: sp.human:*
 - 6: sp.invertebrate:*
 - 7: sp.mammal:*
 - 8: sp.mhc:*
 - 9: sp.organelle:*
 - 10: sp.phage:*
 - 11: sp.plant:*
 - 12: sp.todent:*
 - 13: sp.virus:*
 - 14: sp.unclassified:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	113.5	41.0	461	11	035947 mesocricetu
2	111.5	40.3	298	11	09ESB9 ratius norv
3	111.5	40.3	695	11	09ESB0 ratius norv
4	104.5	37.7	241	6	007112 bos taurus
5	102.5	37.0	111	11	09ESB6 ratius norv
6	102.5	37.0	136	11	09ESB7 ratius norv
7	102.5	37.0	256	11	09ESB6 ratius norv
8	102.5	37.0	317	11	09ESB2 ratius norv
9	102.5	37.0	323	11	09ESB2 ratius norv
10	102.5	37.0	342	11	09ESB1 ratius norv
11	102.5	37.0	700	11	09ESB1 ratius norv
12	102.5	37.0	782	11	09ESB5 ratius norv
13	92.5	33.4	2180	5	001768 caenorhabd
14	89	32.1	162	11	092015 ratius norv
15	89	32.1	1241	4	09UKK5 homo sapien
16	89	32.1	1241	4	09UKD4 homo sapien
17	89	32.1	1241	4	09BZV3 ratius norv
18	88	31.8	1239	11	P70628 ratius norv
19	87	31.4	217	5	09VJV6 drosophila

20	87	31.4	597	11	035727 mus musculus
21	85.5	30.9	1193	13	090819 gallus galli
22	85.5	30.9	1218	4	015122 homo sapien
23	85.5	30.9	1218	4	015816 homo sapien
24	85.5	30.9	1218	4	014902 homo sapien
25	85.5	30.9	1227	4	P78504 homo sapien
26	84.5	30.5	177	11	09JTM4 ratius norv
27	84.5	30.5	1218	11	09QX00 mus musculus
28	84.5	30.5	1219	11	063722 ratius norv
29	83.5	30.1	127	11	09G9F3 ectromella
30	83	30.0	162	11	061521 mus musculus
31	83	30.0	861	11	09QW58 mus sp. mot
32	83	30.0	862	11	09QW58 mus sp. mot
33	82.5	29.8	445	5	09WJMS mus musculus
34	82	29.6	264	5	020559 drosophila
35	80.5	29.1	125	12	041504 cowpox viru
36	80.5	29.1	125	12	09J524 fowlpox vir
37	80.5	29.1	260	4	09S898 homo sapien
38	80.5	29.1	263	4	025253 lucilia cup
39	80	28.9	907	5	09XRS9 caenorhabd
40	79.5	28.7	127	12	041506 bean 58058
41	79.5	28.7	138	12	P87605 cowpox viru
42	79.5	28.7	140	12	057166 vaccinia vi
43	79.5	28.7	140	12	086607 vaccinia vi
44	79.5	28.7	140	12	09JFH4 vaccinia vi
45	79.5	28.7	1581	13	073809 figu rubrip

ALIGNMENTS

RESULT 1

ID 035947 PRELIMINARY: PRT: 461 AA.

AC 035947

DT 01-JAN-1998 (TREMBLrel. 05, Created)

DT 01-JAN-1998 (TREMBLrel. 05, last sequence update)

DT 01-JUN-2001 (TREMBLrel. 17, last annotation update)

DE PRO-NEUREGULIN-1, ISOFORM ALPHA 2B PRECURSOR.

GN NRGI OR NDE.

GN Mesocricetus auratus (Golden hamster).

OC	Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC	Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
OC	Mesocricetus.
OX	NCBI_TaxID=10036;
RN	[1]
RP	SEQUENCE FROM N.A. (ISOFORM ALPHA2B), AND SEQUENCE OF 64-81.
RC	TISSUE=EMBRYO.
RX	MEDLINE=98196996; PubMed=9537646;
RA	Velasco J.A., Feljoo E., Avila M.A., Notario V.;
RT	Secretion of new differentiation factor-like polypeptides by cph-
RT	transformed fibroblasts: cloning and characterization of Syrian
RT	hamster neurogulin cDNAs.";
RL	MOL. Cell Biol. 1998; 18(1):156-163(1998).
CC	-1- FUNCTION: DIRECT LIGAND FOR ERBB3 AND ERBB4 TYROSINE KINASE
CC	RECEPTORS. CONCOMITANTLY RECRUITS ERBB1 AND ERBB2 CORECEPTORS,
CC	RESULTING IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND
CC	ACTIVATION OF THE ERBB RECEPTORS. MAY PLAY AN IMPORTANT ROLE IN
CC	PROVIDING GROWTH ADVANTAGE IN NEOPLASTIC CELLS
CC	-1- SUBUNIT: THE CYTOPLASMIC DOMAIN INTERACTS WITH THE LIM DOMAIN
CC	REGION OF LIMK1 (BY SIMILARITY).
CC	-1- SUBCELLULAR LOCATION: EXISTS AS TYPE I MEMBRANE PROTEIN AND AS A
CC	PROTEOLYTICALLY RELEASED SOLUBLE GROWTH FACTOR FORM. THE MEMBRANE-
CC	BOUND FORM DOES NOT SEEM TO BE ACTIVE (BY SIMILARITY).
CC	-1- ALTERNATIVE PRODUCTS: DIFFERENT ISOFORMS ARE PRODUCED BY
CC	ALTERNATIVE SPLICING. THE SEQUENCE SHOWN IS THAT OF ISOFORM
CC	ALPHA2B/CLONE PM3.
CC	-1- TISSUE SPECIFICITY: EXPRESSED AT HIGHER LEVEL AFTER NEOPLASMIC
CC	TRANSFORMATION OF CELLS.
CC	-1- DOMAIN: THE CYTOPLASMIC DOMAIN MAY BE INVOLVED IN THE REGULATION
CC	OF TRAFFICKING AND PROTEOLYTIC PROCESSING. REGULATION OF THE
CC	PROTEOLYTIC PROCESSING INVOLVES INITIAL INTRACELLULAR DOMAIN
CC	DIMERIZATION (BY SIMILARITY).


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CC -1- DOMAIN: ERBB RECEPTOR BINDING IS ELICITED ENTIRELY BY THE EGF-LIKE
CC DOMAIN.
CC -1- PTM: PROTEOLYTIC CLEAVAGE CLOSE TO THE PLASMA MEMBRANE ON THE
CC EXTERNAL FACE LEADS TO THE RELEASE OF THE SOLUBLE GROWTH FACTOR
CC FORM (BY SIMILARITY).
CC -1- PTM: EXTENSIVE GLYCOSYLATION PRECEDES PROTEOLYTIC CLEAVAGE (BY
CC SIMILARITY).
CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
CC -1- SIMILARITY: CONTAINS 1 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAIN.
CC EMBL: U96612; AAB71812.1; -.
DR HSP: Q12784; IHR.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR003598; I9_C2.
DR InterPro: IPR003006; I9_MHC.
DR Pfam: PF00008; EGF_1.
DR InterPro: IPR002154; Neuregulin.
DR Pfam: PF02158; Neuregulin; 1.
DR PRINTS: PRO1089; NEUREGULIN.
DR SMART: SM00181; EGF; 1.
DR SMART: SM00408; IGC2; 1.
DR PROSITE: PS00022; EGF_1; UNKNOWN_1.
DR PROSITE: PS01186; EGF_2; 1.
KM Growth factor: EGF-like domain; Immunoglobulin domain; Glycoprotein;
KW Transmembrane; Alternative splicing.
FT PROPER 1 13
FT CHAIN 14 461
FT CHAIN 14 241
FT DOMAIN 14 242
FT TRANSMEM 243 265
FT DOMAIN 266 461
FT DOMAIN 50 119
FT DOMAIN 165 177
FT DOMAIN 178 222
FT DISULFID 57 112
FT DISULFID 182 196
FT DISULFID 190 210
FT DISULFID 212 221
FT CARBOHYD 73 77
FT CARBOHYD 120 120
FT CARBOHYD 126 126
FT CARBOHYD 164 164
SQ SEQUENCE 461 AA; 50890 MW; 935C9560F7148336 CRC64;

Query Match 41.0%; Score 113.5; DB 11; Length 461;
Best Local Similarity 34.8%; Pred. No. 3.2e-07;
Matches 16; Conservative 14; Mismatches 15; Indels 1; Gaps 1;

OY 1 HFRPCRDKLAVCLNDGCEFTVETLTGSHKH-CRCKEGYGVRCDO 45
DB 178 HLYKCAKEKTEPCVNGGCEFTVADLSNPSRYLCKCPGFTGARCTE 223

RESULT 2
OQESB9 PRELIMINARY; PRT; 298 AA.
AC OQESB9;
DT 01-MAR-2001 (TREMblrel. 16, Created)
DT 01-MAR-2001 (TREMblrel. 16, Last sequence update)
DE SMDP NEUREGULIN ALPHA 2B (FRAGMENT).
GN NRGI.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN-BDIX;
RA Carroll S.L., Anderson K.D., Frohner P.W.;
RT "Structural and Functional Diversity of SMDP Neuregulin Splice

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RT Variants Expressed in the Adult Rat Nervous System.
RT Submitted (OCT-1999) to the EMBL/Genbank/DBD databases.
DR EMBL: AF194440; AAG28429.1; -.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR002154; Neuregulin.
DR InterPro: IPR002114; PTS_HPT_ser.
DR Pfam: PF00008; EGF; 1.
DR Pfam: PF02158; Neuregulin; 1.
DR PRINTS: PRO1089; NEUREGULIN.
DR SMART: SM00181; EGF; 1.
DR SMART: SM00001; EGF-like; 1.
DR PROSITE: PS00022; EGF_1; UNKNOWN_1.
DR PROSITE: PS00589; PTS_HPT_ser; UNKNOWN_1.
FT NON_TER 1 298
FT TER 298
SQ SEQUENCE 298 AA; 32851 MW; BD76F014C2B33026 CRC64;

Query Match 40.3%; Score 111.5; DB 11; Length 298;
Best Local Similarity 34.8%; Pred. No. 3.9e-07;
Matches 16; Conservative 13; Mismatches 16; Indels 1; Gaps 1;

OY 1 HFRPCRDKLAVCLNDGCEFTVETLTGSHKH-CRCKEGYGVRCDO 45
DB 48 HLYKCAKEKTEPCVNGGCEFTVADLSNPSRYLCKCPGFTGARCTE 93

RESULT 3
OQESB0 PRELIMINARY; PRT; 695 AA.
AC OQESB0;
DT 01-MAR-2001 (TREMblrel. 16, Created)
DT 01-MAR-2001 (TREMblrel. 16, Last sequence update)
DE SMDP NEUREGULIN ALPHA 2A.
GN NRGI.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN-BDIX;
RA Carroll S.L., Anderson K.D., Frohner P.W.;
RT "Structural and Functional Diversity of SMDP Neuregulin Splice
RT Variants Expressed in the Adult Rat Nervous System.
RT Submitted (OCT-1999) to the EMBL/Genbank/DBD databases.
DR EMBL: AF194439; AAG28428.1; -.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR002154; Neuregulin.
DR InterPro: IPR002114; PTS_HPT_ser.
DR Pfam: PF00008; EGF; 1.
DR Pfam: PF02158; Neuregulin; 1.
DR PRINTS: PRO1089; NEUREGULIN.
DR SMART: SM00181; EGF; 1.
DR SMART: SM00001; EGF-like; 1.
DR PROSITE: PS00022; EGF_1; UNKNOWN_1.
DR PROSITE: PS00589; PTS_HPT_ser; UNKNOWN_1.
SQ SEQUENCE 695 AA; 75646 MW; 5277F2CBA2FB6878 CRC64;

Query Match 40.3%; Score 111.5; DB 11; Length 695;
Best Local Similarity 34.8%; Pred. No. 8.8e-07;
Matches 16; Conservative 13; Mismatches 16; Indels 1; Gaps 1;

OY 1 HFRPCRDKLAVCLNDGCEFTVETLTGSHKH-CRCKEGYGVRCDO 45
DB 234 HLYKCAKEKTEPCVNGGCEFTVADLSNPSRYLCKCPGFTGARCTE 279

RESULT 4
OQ7112 PRELIMINARY; PRT; 241 AA.
ID OQ7112

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AC 007112; (TREMBLER, 05, Created)
 DT 01-JAN-1998 (TREMBLER, 05, Last sequence update)
 DT 01-JUN-2001 (TREMBLER, 17, Last annotation update)
 DE NEUREGULIN-1, GLIAL GROWTH FACTOR 5 ISOFORM PRECURSOR (GGBPP5).
 GN NRGI OR GGF.
 OS Bos taurus (Bovine).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovidea;
 OC Bovidae; Bovinae; Bos.
 OC NCBI_TaxID=9913;
 RN [1]
 RP SEQUENCE FROM N.A., AND PARTIAL SEQUENCE.
 RC TISSUE-POSTERIOR PITUITARY;
 RX MEDLINE=9305115; PubMed=8096067;
 RA Marchionni M.A., Goodheart A.D.J., Chen M.S., Bermingham-McDonogh O.,
 RA Kirt C., Hendricks M., Daneshy F., Misumi D., Sudhalter J.,
 RA Kobayashi K., Wroblewski D., Lynch C., Baldeasarre M., Hiles I.,
 RA Davis J.B., Hsuan J.J., Tolly N.F., Otsu M., McBurney K.N.,
 RA Waterfield M.D., Stroobant P., Gwynne D.;
 RT "Glial growth factors are alternatively spliced exons 2 ligands
 expressed in the nervous system."
 RL Nature 362:312-318(1993).
 CC -1- FUNCTION: DIRECT LIGAND FOR ERBB3 AND ERBB4 TYROSINE KINASE
 RECEPTORS. CONCOMITANTLY RECRUITS ERBB1 AND ERBB2 CORECEPTORS,
 CC RESULTING IN LIGAND-STIMULATED TYROSINE PHOSPHORYLATION AND
 CC ACTIVATION OF THE ERBB RECEPTORS (BY SIMILARITY).
 CC -1- SUBCELLULAR LOCATION: SECRETED (PROBABLE).
 CC -1- TISSUE SPECIFICITY: EXPRESSED IN NERVOUS SYSTEM: SPINAL CORD AND
 CC BRAIN.
 CC -1- ALTERNATIVE PRODUCTS: AT LEAST FIVE DIFFERENT ISOFORMS: GGBPP1,
 CC GGBPP2, GGBPP3, GGBPP4 AND GGBPP5 (SHOWN HERE); ARE PRODUCED
 CC BY ALTERNATIVE SPLICING.
 CC -1- SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
 CC -1- SIMILARITY: CONTAINS 1 IMMUNOGLOBULIN-LIKE C2-TYPE DOMAIN.
 CC EMBL: L12259; AAA30540.1; -
 DR HSSP: Q12784; IIRE.
 DR Interpro: IPR000561; EGF-like.
 DR Interpro: IPR003598; Iq_C2.
 DR Interpro: IPR003006; Iq_MHC.
 DR Pfam: PF00008; EGF; 1.
 DR Pfam: PF00047; Iq; 1.
 DR SMART: SM00181; EGF; 1.
 DR SMART: SM00408; ICG2; 1.
 DR PROSITE: PS00022; EGF_1; UNKNOWN_1.
 DR PROSITE: PS01186; EGF_2; FALSE_NEG.
 DR Growth factor; EGF-like domain; Immunoglobulin domain;
 DR Alternative splicing.
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CC      DOMAININ.
DR      EMBL; AF194995; AAG28449.1; -.
DR      InterPro; IPR000561; EGF-like.
DR      InterPro; IPR000886; ER_target.
DR      InterPro; IPR003599; IG.
DR      InterPro; IPR003598; IG_C2.
DR      InterPro; IPR003006; IG_MHC.
DR      Pfam; PF00008; EGF_1.
DR      Pfam; PF00047; Ig_1.
DR      SMART; SM00181; EGF_1.
DR      SMART; SM00001; EGF_like_1.
DR      SMART; SM00409; IG_1.
DR      SMART; SM00408; IGC2_1.
DR      PROSITE; PS00014; ER_TARGET; UNKNOWN_1.
FT      NON_TER
TT      1
SQ      SEQUENCE          317 AA;  34785 MW;  4487FA3E9CD876B9 CRC64;

Query Match                      37.0%; Score 102.5; DB 11; Length 317;
Best Local Similarity            31.2%; Pred. No. 6,7e-06;
Matches    15; Conservative     13; Mismatches   19; Indels    1; Gaps        1

QY      1 HRPCKDQLAYCLNDCEPVLETLGSHKH-CRCKEGYGVCADQFL 47
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RESULT         9

ID QGESA2             PRELIMINARY;           PRT;       323 AA.
AC QGESA2;
DT 01-MAR-2001 (TREMBlrel. 16, Created)
DT 01-MAR-2001 (TREMBlrel. 16, last sequence update)
DE 01-JUN-2001 (TREMBlrel. 17, last annotation update)
DE GLIAL GROWTH FACTOR GCF BETA 3 (FRAGMENT).
GN NRG1
OS Rattus norvegicus (Rat.).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_Taxid=10116;
RN [1]
RC
FP STRAIN=SPRAGUE-DAWLEY;
RA Carroll S.L., Stonecypher M.S., Anderson K.D., Pearson R.J. Jr.,
RA Frommert P.W.;
RT "Structural and Functional Diversity of Glial Growth Factor Isoforms
RT Expressed in Regenerating Peripheral Nerve and Associated Neurons.";
RL Submitted (OGC1999) to the EMBL/Genebank/DDBJ databases.
CC -1 SIMILARITY: TO IMMUNOGLOBULIN AND MAJOR HISTOCOMPATIBILITY COMPLEX
CC DOMAININ.
CC EMBL; AF194996; AAG28450.1; -.
DR      InterPro; IPR000561; EGF-like.
DR      InterPro; IPR003599; IG.
DR      InterPro; IPR003598; IG_C2.
DR      InterPro; IPR003600; IG_like.
DR      InterPro; IPR003006; IG_MHC.
DR      Pfam; PF00008; EGF_1.
DR      Pfam; PF00047; Ig_1.
DR      SMART; SM00181; EGF_1.
DR      SMART; SM00001; EGF_like_1.
DR      SMART; SM00409; IG_1.
DR      SMART; SM00408; IGC2_1.
DR      SMART; SM00410; IG_like_1.
DR      PROSITE; PS00022; EGF_1; UNKNOWN_1.
FT      NON_TER
TT      1
SQ      SEQUENCE          323 AA;  35358 MW;  C7DF153A939A80C8 CRC64;
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QY 1 HRRPCDKLALYCLNDGECFVIEITLGSNKH-CRCKEGYGVRCDOFL 47
 DB 316 HLIKAEKERTFCVNGCEFTVKDLNPSRNYLCKCPNEFTGRCONYV 363

RESULT 13
 ID 001768 PRELIMINARY; PRT: 2180 AA.
 AC 001768;
 DT 01-JUL-1997 (Tremblrel. 04, Created)
 DT 01-JUL-1997 (Tremblrel. 04, Last sequence update)
 DT 01-JUN-2001 (Tremblrel. 17, Last annotation update)
 DE HYPOPHYSEAL 241.7 KDA PROTEIN T21E3.3 IN CHROMOSOME 1.
 GN T21E3.3.
 OS Caenorhabditis elegans.
 OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditidae;
 OC Rhabditidae; Peloderinae; Caenorhabditis.
 OX NCBI_TaxID=6239;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC STRAIN-BRISTOL N2;
 RL Du 2., Le T.T.;
 RL Submitted (MAY-1997) to the EMBL/Genbank/DBJ databases.
 CC -1 SIMILARITY: TO LOW DENSITY LIPOPROTEIN (LDL) RECEPTOR CLASS A
 (LDLR) DOMAIN
 DR EMBL: AF003133; AAB54138.1; -
 DR HSSP: Q07954; ICR8.
 DR InterPro: IPR000561; EGF-like.
 DR InterPro: IPR002049; Laminin_EGF.
 DR InterPro: IPR000033; LDL_receptor_rep.
 DR InterPro: IPR002172; LDL_receptor_A.
 DR Pfam: PF00008; EGF_9.
 DR Pfam: PF00057; LDL_receptor_a; 18.
 DR Pfam: PF00058; LDL_receptor_b; 8.
 DR PRINTS: PR00011; EGF_LAMININ.
 DR PRINTS: PR00261; LDLRECEPTOR.
 DR SMART: SM00181; EGF; 10.
 DR SMART: SM00192; LDLa; 20.
 DR SMART: SM00135; LY; 7.
 DR PROSITE: PS00022; EGF_1; UNKNOWN_9.
 DR PROSITE: PS01186; EGF_2; 7.
 DR PROSITE: PS01209; LDLRA_1; 10.
 DR PROSITE: PS00068; LDLRA_2; 21.
 KW EGF-like domain; Glycoprotein; Hypothetical protein.
 SO SEQUENCE 2180 AA; 241705 MW; C26419F456A60D13 CRC64;

Query Match 33.4%; Score 92.5; DB 5; Length 2180;
 Best Local Similarity 42.9%; Pred. No. 0.00092;
 Matches 18; Conservative 8; Mismatches 7; Indels 9; Gaps 3;

OY 5 CRDKLALYCLNDGECFVIEITLGSNKHCRCKEGYGVRCDOFL 45
 DB 1906 CDD-----YCTNNSKC-----TITNGTHRECDCKPFGKLRCEQ 1939

RESULT 14
 ID 0920L5 PRELIMINARY; PRT: 162 AA.
 AC 0920L5;
 DT 01-MAY-1999 (Tremblrel. 10, Created)
 DT 01-MAY-1999 (Tremblrel. 10, Last sequence update)
 DT 01-JUN-2001 (Tremblrel. 17, Last annotation update)
 DE PERIGULIN PRECURSOR.
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_TaxID=10116;
 RN [1]
 RP SEQUENCE FROM N.A.; SEQUENCE OF 56-75, AND CHARACTERIZATION.
 RC TISSUE-AORTIC SMOOTH MUSCLE;
 RX MEDLINE=99145602; PubMed=9990076;
 RA Taylor D.S., Cheng X., Pawlowski J.E., Wallace A.R., Ferrer P.,

RA Molloy C.J.;
 RT "Epitregulin is a potent vascular smooth muscle cell-derived mitogen
 induced by angiotensin II, endothelin-1, and thrombin";
 RL Proc. Natl. Acad. Sci. U.S.A. 96:1633-1638(1999).
 CC -1 FUNCTION: MAY BE A MEDIATOR OF LOCALIZED CELL PROLIFERATION. AS A
 MITOGEN IT MAY STIMULATE CELL PROLIFERATION AND/OR ANGIOGENESIS.
 CC -1 SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN (PRECURSOR FORM);
 CC EXTRACELLULAR (MATURE FORM).
 CC -1 SIMILARITY: CONTAINS 1 EGF-LIKE DOMAIN.
 DR EMBL: AF074952; AAD10631.1; -
 DR InterPro: IPR000561; EGF-like.
 DR InterPro: IPR001336; EGF_1.
 DR PRINTS: PR00009; EGFTEF.
 DR SMART: SM00181; EGF; 1.
 DR PROSITE: PS00022; EGF_1; UNKNOWN_1.
 DR PROSITE: PS01186; EGF_2; 1.
 KW Growth factor; Mitogen; Glycoprotein; EGF-like domain; Transmembrane;
 KM Signal.
 FT SIGNAL 1 22 POTENTIAL.
 FT PROPER 23 55 POTENTIAL.
 FT CHAIN 56 101 EPIREGULIN.
 FT PROPEP 102 162 REMOVED IN MATURE FORM (BY SIMILARITY).
 FT DOMAIN 56 112 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 113 133 POTENTIAL.
 FT DOMAIN 134 162 CYTOPLASMIC (POTENTIAL).
 FT DOMAIN 138 145 ARC/LYS-RICH (BASIC).
 FT CARBOHYD 40 40 N-LINKED (GLCNAC. .) (POTENTIAL).
 FT DOMAIN 57 97 EGF-LIKE.
 FT DISULFID 61 74 BY SIMILARITY.
 FT DISULFID 69 85 BY SIMILARITY.
 FT DISULFID 87 96 BY SIMILARITY.
 SO SEQUENCE 162 AA; 18404 MW; EA660DEB34990C4 CRC64;

Query Match 32.1%; Score 89; DB 11; Length 162;
 Best Local Similarity 45.0%; Pred. No. 0.00023;
 Matches 18; Conservative 7; Mismatches 11; Indels 4; Gaps 3;

OY 7 DKDLALYCLNDGECFVIEITLGSNKHCRCKEGYGVRCDOFL 46
 DB 64 DMD-GYCLH-GHCYLVDM--SEKYCRCEVGYGLRCEHF 99

RESULT 15
 ID 090RK5 PRELIMINARY; PRT: 1241 AA.
 AC 090RK5;
 DT 01-MAY-2000 (Tremblrel. 13, Created)
 DT 01-MAY-2000 (Tremblrel. 13, Last sequence update)
 DT 01-JUN-2001 (Tremblrel. 17, Last annotation update)
 DE SPACRCAN.
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Acharya S., Foleta V.C., Lee J.W., Rayborn M.E., Rodriguez I.R.,
 RA Young W.S., Hollifield J.G.;
 RT "SPACRCAN, a novel human interphotoreceptor matrix hyaluronan-binding
 RT proteoglycan synthesized by photoreceptors and pinealocytes";
 RL Submitted (JUN-1999) to the EMBL/Genbank/DBJ databases.
 DR EMBL: AF157624; AAF13154.1; -
 DR InterPro: IPR000082; SEA.
 DR InterPro: IPR000561; EGF-like.
 DR Pfam: PF01390; SEA; 2.
 DR PROSITE: PS01186; EGF_2; UNKNOWN_1.
 DR SMART: SM00200; SEA; 2.
 SO SEQUENCE 1241 AA; 138605 MW; 1F3AE3DB39F8858 CRC64;

Query Match 32.1%; Score 89; DB 4; Length 1241;
 Best Local Similarity 34.6%; Pred. No. 0.0016;

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	Matches	18;	Conservative	11;	Mismatches	13;	Indels	10;	Gaps	3.
QY	3	KPCR---	DKDLAYCNDGECFYERTLWGSKHKRCKEG----	YGVRDQDL	47					
	:	11:	:	: :	11:	:	1:1	1:1:		
Db	1048	RPCOSLCLOPDPFCINDKC--	-DIMPGHGAICRCRVGENWYRGKHCEEFV	1096						

Search completed: February 7, 2002, 13:03:00
Job time: 188 sec